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NB: This Note contains tables, boxes, case histories, schemes, diagrams, algorithms and summaries in Lissauer textbook included in fifth year curriculum.

Chapter 2: History and examination

Table 2-1. Respiratory rate in children (breaths/min)

Age	Normal	Tachypnoea
Neonate	30-50	>60
Infants	20-30	>50
Young children	20-30	>40
Older children	15-20	>30

Table 2-2. Chest signs of some common chest disorders of children

	Chest movement	Percussion	Auscultation
Bronchiolitis	Laboured breathing Hyperinflated chest	Hyper-resonant	Fine crackles in all zones
	Chest recession		Wheezes may/may not be present
Pneumonia	Reduced on affected side	Dull	Bronchial breathing
	Rapid, shallow breaths		Crackles
Asthma	Reduced but hyperinflated	Hyper-resonant	Wheeze
	Use of accessory muscles		
	Chest wall retraction		

- **Sputum is rarely produced by children, as they swallow it. The main exception is suppurative lung disease from cystic fibrosis.**

Cardiovascular system

Table 2-3. Normal resting pulse rate in children

Age	Beats/min
<1 year	110-160
2-5 years	95-140
5-12 years	80-120
>12 years	60-100

- **Features of heart failure in infants:**
  - **Poor feeding/failure to thrive**
  - **Sweating**
  - **Tachypnoea**
  - **Tachycardia**
  - **Gallop rhythm**
  - **Cardiomegaly**
  - **Hepatomegaly.**

- **Features suggesting that a murmur is significant:**
  - **Conducted all over the precordium**
  - **Loud**
  - **Thrill (equals grade 4-6 murmur)**
  - **Any diastolic murmur**
  - **Accompanied by other abnormal cardiac signs.**

Abdomen

Table 2-4. Causes of hepatomegaly

Infection	Congenital, infectious mononucleosis, hepatitis, malaria, parasitic infection
Haematological	Sickle cell anaemia, thalassaemia
Liver disease	Chronic active hepatitis, portal hypertension, polycystic disease
Malignancy	Leukaemia, lymphoma, neuroblastoma, Wilms' tumour, hepatoblastoma
Metabolic	Glycogen and lipid storage disorders, mucopolysaccharidoses
Cardiovascular	Heart failure
Apparent	Chest hyperexpansion from bronchiolitis or asthma

- **On examining the abdomen:**
  - **Inspect first, palpate later**
  - **Superficial palpation first, deep palpation later**
  - **Guarding is unimpressive in children**
  - **Silent abdomen - serious!**
  - **Immobile abdomen - serious!**

Table 2-5. Causes of splenomegaly

Infection	Viral, bacterial, protozoal (malaria, leishmaniasis), parasites, infective endocarditis
Haematological	Haemolytic anaemia
Malignancy	Leukaemia, lymphoma
Other	Portal hypertension, systemic juvenile idiopathic arthritis (Still's disease)

Cranial nerves

I	Need not be tested in routine practice. Can be done by recognising the smell of a hidden mint sweet.
II	Visual acuity - determined according to age. Direct and consensual pupillary response tested to light and accommodation. Visual fields can be tested if the child is old enough to cooperate.
III, IV, VI	Full eye movement through horizontal and vertical planes. Is there a squint? Nystagmus - avoid extreme lateral gaze, as it can induce nystagmus in normal children.
V	Clench teeth and waggle jaw from side to side against resistance.
VII	Close eyes tight, smile and show teeth.
VIII	Hearing - ask parents, although unilateral deafness could be missed this way. If in doubt, needs formal assessment in a suitable environment.
IX	Levator palati - saying 'aagh'. Look for deviation of uvula.
X	Recurrent laryngeal nerve - listen for hoarseness or stridor.
XI	Trapezius and sternomastoid power - shrug shoulders and turn head against resistance.
XII	Put out tongue and look for any atrophy or deviation.

pGALS – musculoskeletal screening for school-aged children

(Differences from adult GALS highlighted in bold)

Screening questions

- **Do you (or your child) have any pain or stiffness in your joints, muscles or your back?**
- **Do you (or your child) have any difficulty getting yourself dressed without any help?**
- **Do you (or your child) have any difficulty going up and down stairs?**

POSTURE AND GAIT

Observe standing (from front, back and sides)

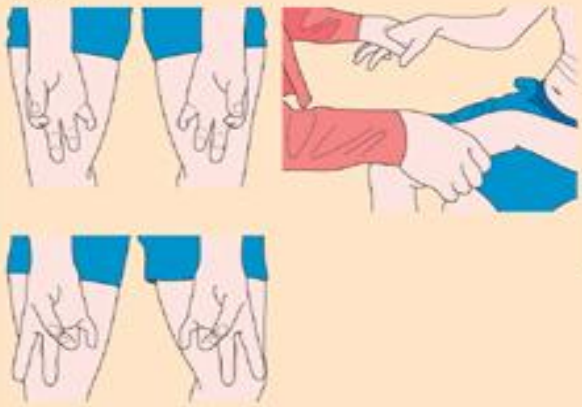
Observe walking **'Walk on your tip-toes, walk on your heels'**

ARMS

'Put your hands out straight in front of you'

'Turn your hands over and make a fist'

ARMS



'Pinch your index finger and thumb together'

'Touch the tips of your fingers with your thumb'

Squeeze the metacarpo-phalangeal joints for tenderness

'Put your hands together palm to palm'

'Put your hands back to back'

'Reach up and touch the sky'

'Look at the ceiling'

Figure 2.10 pGALS (paediatric Gait, Arms, Legs, Spine) musculoskeletal screening for school-aged children

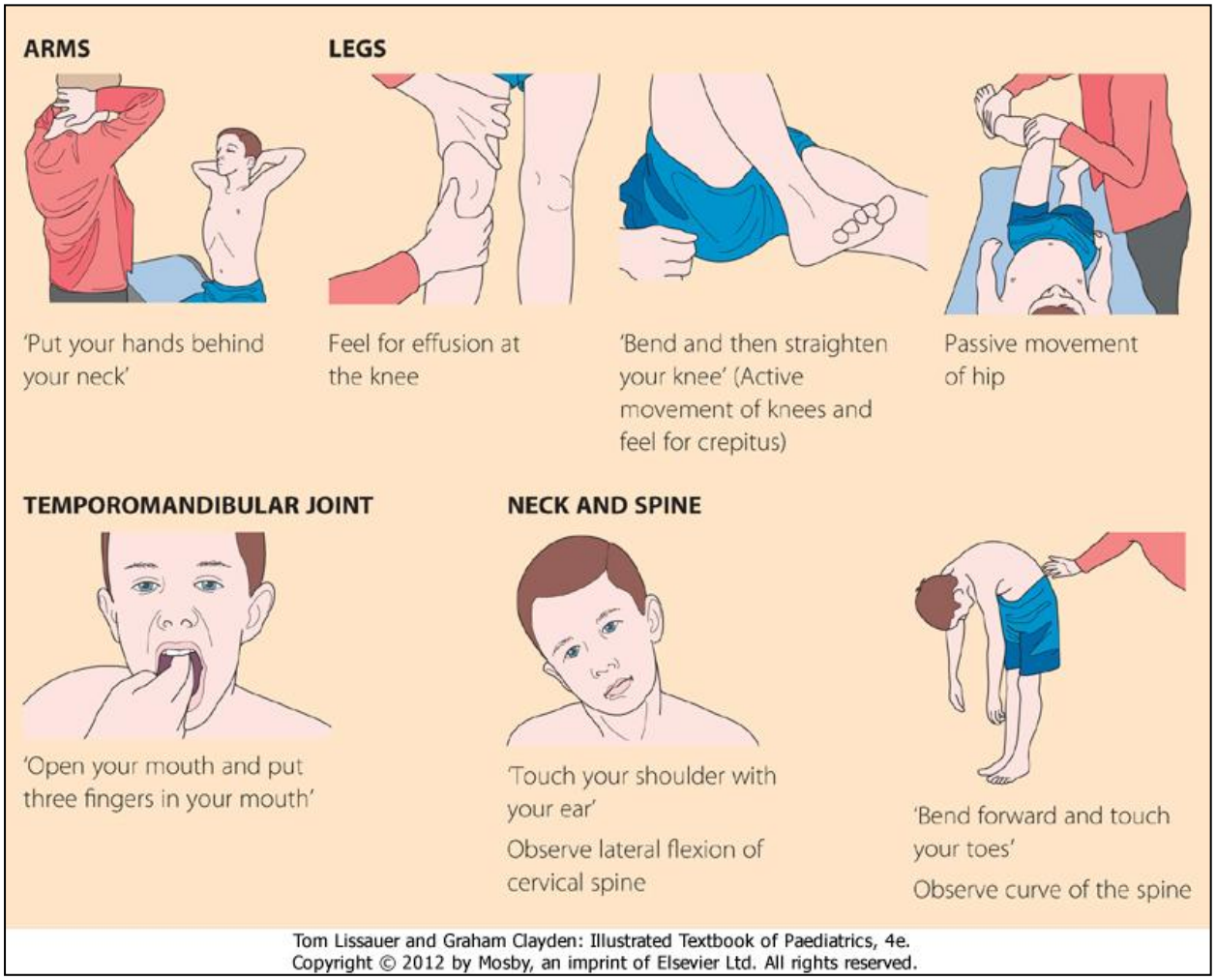


Figure 2.10 pGALS (paediatric Gait, Arms, Legs, Spine) musculoskeletal screening for school-aged children

Regional musculoskeletal assessment

Look:
- For signs of discomfort
- Skin abnormalities – rashes, scars, bruising, colour, nail abnormalities
- Limb alignment, leg length, muscle bulk and evidence of asymmetry
- Bony deformity, soft tissue, joint swelling or muscle changes

Feel:
- Each joint, long bones and neighbouring soft tissues:
- Palpate along bones and joint line for tenderness
- Feel for warmth ***(infection or inflammation)***
- Delineate bony or soft tissue swellings
- Check for joint effusion, most readily at the knee

Move:
- For each joint, ask to move the joint first (active movement).
  Observe for discomfort, symmetry and range of movement.
- Passively move the joint, noting range of any restriction of movement (compare sides but note bilateral changes)
- Lateral and rotational movements may be as important as flexion and extension.

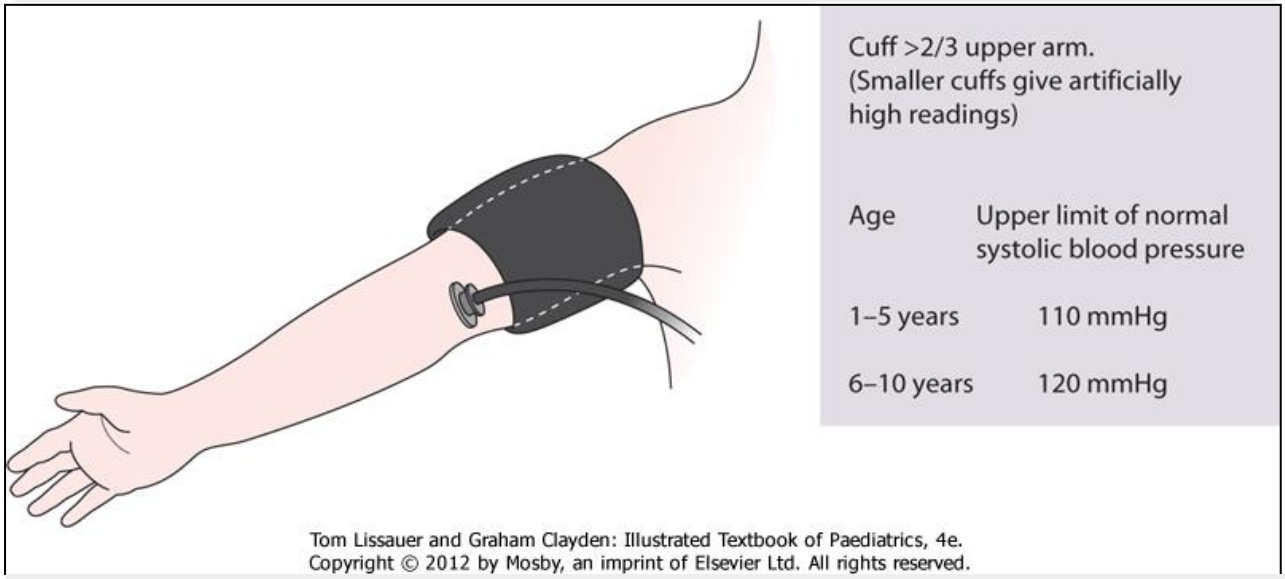
Function:
- For lower limb joints – check gait
- For small joints such as hands - check grip

Table 2-6. The reasons for talking with children

	Why talk to children when you can get the information from the parent? The reasons are: • To establish rapport • To obtain the child's own views about their problems • To know how the child feels about their health and life • To reduce anxiety and fear and to improve compliance with assessment and treatment • To determine the presence of associated emotional or psychiatric problems		
	Preschool child (2-5 years)	**School-age child (6-11 years)**	**Adolescent (12-18 years)**
Thought processes	When I close my eyes, Mum goes away (world viewed differently, from own perspective) I am asleep, so everyone is asleep (centre of their world) When I fell, the floor hurt me (objects are alive) My toy elephant is crying because the other elephants won't play with him (involvement in pretend play) 	I have been invited to Katie and Jane's parties - maybe I could go for some time to each (able to start solving concrete problems) Am I going to be chosen for the school choir? (develops worries about the future) Mum gets really upset when Dad gets drunk, but Dad does not care (able to see another person's point of view and take on more than one perspective) 	I can handle things without Mum's help (seeking autonomy and separation) Should our country be at war? (develops concern about social issues) 
Effect on the way we talk to them	Use short, concrete questions within their immediate experience. To avoid yes/no answers use a choice of options, e.g. when you go to nursery, what do you like to do - draw or dress up or something else? Use toys or puppets while interviewing, e.g. to represent different people in the child's life	Use familiar examples of experience of others to explore the child's feelings and behaviour, e.g. when a boy was bullying another boy at school, he came to see me so we could talk about how he controls his temper. Do you ever get angry and bully others? You can get at their hopes and dreams by asking them, 'If I was a magician and could give you three wishes, what would they be?'	Should be given an opportunity to be seen alone as they may have problems and difficulties not known to the parents and that the adolescent does not want to share with them Upsetting thoughts can be explored in some adolescents using metaphors

Box 2.1 Measuring blood pressure in children

- Sphygmomanometer (Fig. 2.12)
  - - stethoscope in older children
  - - Doppler ultrasound in infants
- Oscillometric (e.g. Dynamapp) - unreliable in infants and young children
- Invasive - direct measurement from an arterial catheter is preferable if critically ill.



Cuff >2/3 upper arm.
(Smaller cuffs give artificially high readings)

Age	Upper limit of normal systolic blood pressure
1–5 years	110 mmHg
6–10 years	120 mmHg

Summary

In taking a history and performing a clinical examination:

- The child's age is a key feature - it will determine the nature of the problem, how the consultation is conducted, the likely diagnosis and its management.
- The interview environment should be welcoming - with suitable toys for young children.
- Most information is usually obtained from a focused history and observation, rather than detailed examination although examination is also important.
- Check growth, including charts in personal child health record, and development.
- With young children - be confident but gentle, do not ask their permission to examine them or they may say 'no', and leave unpleasant procedures (ears and throat) until last.
- Involve children with the consultation, as appropriate to their age.

Remember child protection when taking a history or examining a child where there are unusual findings.

Chapter 3: Normal child development, hearing and vision

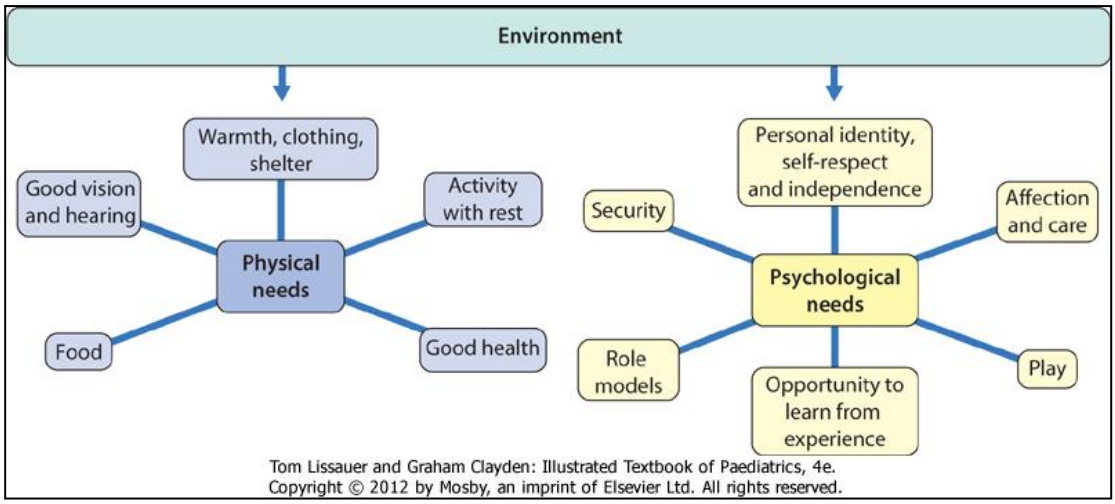


Figure 3.1 Development can be impaired if the environment fails to meet the child's physical or psychological needs.

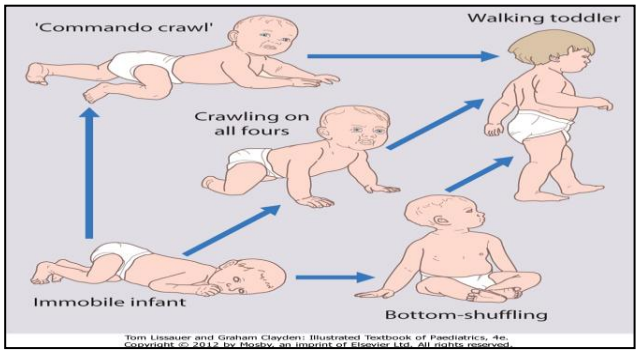


Figure 3.3 Early locomotor patterns. Most children crawl on all fours prior to walking, but some 'bottom-shuffle' and others 'commando crawl' (creep). Bottom-shuffling often runs in families. The late walking that often goes with this locomotor variant needs to be differentiated from an abnormality such as cerebral palsy.

Summary

Assessing child development

When assessing a young child's development:

- Consider the four fields of developmental skills: gross motor; vision and fine motor; hearing, speech and language; social, emotional, behavioural
- The acquisition of developmental abilities follows a similar pattern between children, but may vary in rate, and still be normal.

Terms used are:

- Developmental milestones: the acquisition of important developmental skills
- Median age - when half the population acquire a skill; serves as a guide to normal pattern of development
- Limit age - when a skill should have been acquired; further assessment is indicated if not achieved.

When evaluating a child's development, consider:

- the sequence of developmental progress
- the stage the child has reached for each skill field
- if progress is similar in each skill field
- how the child's developmental achievements relate to age.

Table 3-1. The primitive reflexes present at birth gradually disappear as postural reflexes develop, which are essential for independent sitting and walking

Primitive reflexes	Postural reflexes
Moro - sudden extension of the head causes symmetrical extension, then flexion of the arms	**Labyrinthine righting** - head moves in opposite direction to which the body is tilted
Grasp - flexion of fingers when an object is placed in the palm **Rooting** - head turns to the stimulus when touched near the mouth **Stepping response** - stepping movements when held vertically and dorsum of feet touch a surface **Asymmetrical tonic neck reflex** - lying supine, the infant adopts an outstretched arm to the side to which the head is turned	**Postural support** - when held upright, legs take weight and may push up (bounce) **Lateral propping** - in sitting, the arm extends on the side to which the child falls as a saving mechanism **Parachute** - when suspended face down, the arms extend as though to save themself

Summary
Developmental milestones by median age

Age	Gross motor	Vision and fine motor	Hearing, speech and language	Social, emotional and behavioural
Newborn	Flexed posture	Fixes and follows face	Stills to voice	Smiles - by 6 weeks
			Startles to loud noise	
7 months	Sits without support	Transfers objects from hand to hand	Turns to voice Polysyllabic babble	Finger feeds Fears strangers
1 year	Stands independently	Pincer grip (10 months)	1-2 words Understands name	Drinks from cup Waves
		Points		
15-18 months	Walks independently	Immature grip of pencil Random scribble	6-10 words Points to four body parts	Feeds self with spoon Beginning to help with dressing
2½years	Runs and jumps	Draws	3-4 word sentences Understands two joined commands	Parallel play Clean and dry

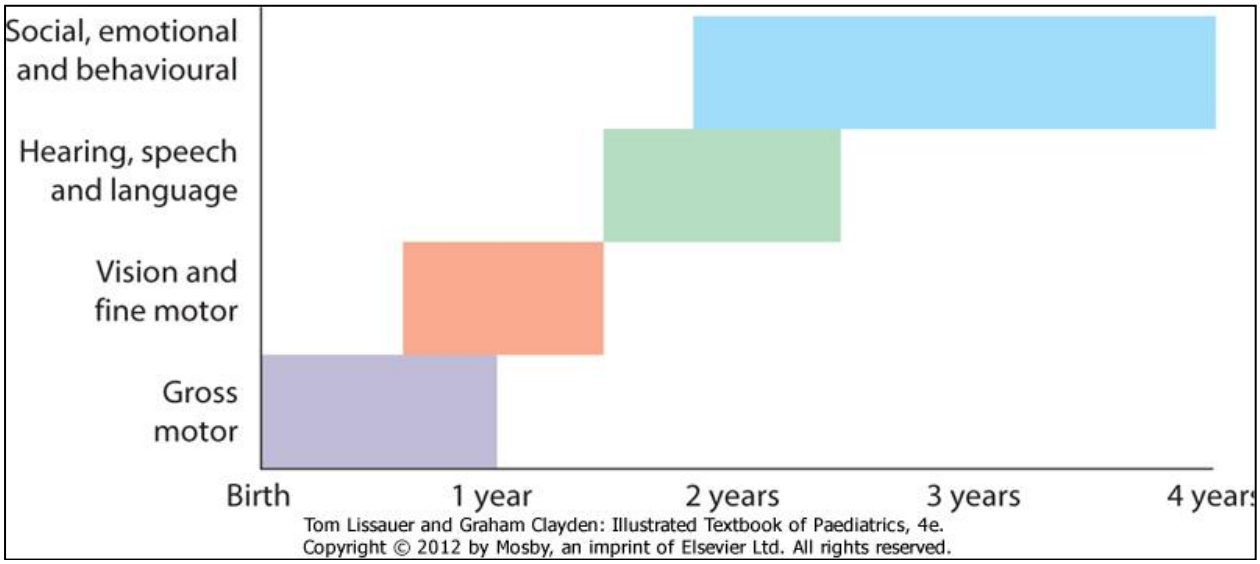


Figure 3.8 Diagram highlighting the ages when there is the most rapid emergence of skills in each developmental field.

Gross motor development (median ages)

newborn

Limbs flexed, symmetrical posture

newborn

Marked head lag on pulling up

6–8 weeks

Raises head to 45° in prone

6–8 months

Sits without support
– at 6 months: with round back
– at 8 months: with straight back (shown)

8–9 months

Crawling

10 months

Cruises around furniture

12 months

Walks unsteadily,
broad gait, hands apart

15 months

Walks steadily

Vision and fine motor (median ages)

6 weeks

Follows moving object or face by turning the head (illustrated).

4 months

Reaches out for toys

4–6 months

Palmar grasp

7 months

Transfers toys from one hand to another

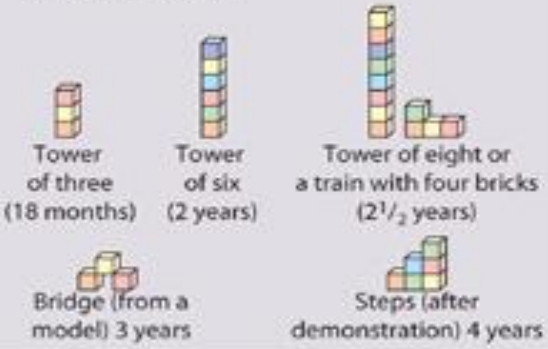
10 months

Mature pincer grip

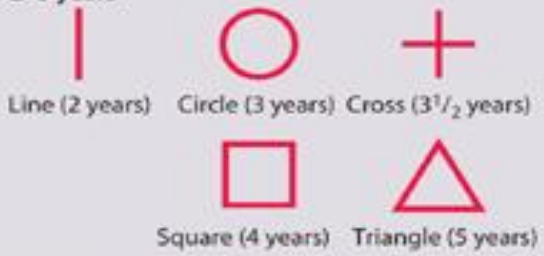
16–18 months

Makes marks with a crayon

14 months–4 years



2–5 years



Ability to draw without seeing how it is done. Can copy (draw after seeing it done) 6 months earlier.

Hearing, speech and language (median ages)

(a) NEWBORN

Startles to loud noises

(b) 3–4 MONTHS

Vocalises alone or when spoken to, coos and laughs

(c) 7 MONTHS

Turns to soft sounds out of sight

(d) 7–10 MONTHS

At 7 months, sounds used indiscriminately. At 10 months, sounds used discriminately to parents

(e) 12 MONTHS

Two to three words other than 'dada' or 'mama'

(f) 18 MONTHS

6–10 words. Shows two parts of the body

(g) 20–24 MONTHS

Uses two or more words to make simple phrases

(h) $2^1/_2$–3 YEARS

Talks constantly in 3–4 word sentences

Social, emotional and behavioural development (median ages)

(a) 6 WEEKS

Smiles responsively

(b) 6–8 MONTHS

Puts food in mouth

(c) 10–12 MONTHS

Waves bye-bye, plays peek-a-boo

(d) 12 MONTHS

Drinks from a cup with two hands

(e) 18 MONTHS

Holds spoon and gets food safely to mouth

(f) 18–24 MONTHS

Symbolic play

(g) 2 YEARS

Dry by day. Pulls off some clothing

(h) 2.5–3 YEARS

Parallel play. Interactive play evolving. Takes turn

Summary

Fields of development with limit ages

Gross motor development

- Acquisition of tone and head control
- Primitive reflexes disappear
- Sitting
- Locomotor patterns
- Standing, walking, running
- Hopping, jumping, peddling

Gross motor	Limit ages
Head control	4 months
Sits unsupported	9 months
Stands independently	12 months
Walks independently	18 months

Vision and fine motor development

- Visual alertness, fixing and following
- Grasp reflex, hand regard
- Voluntary grasping, pincer, points
- Handles objects with both hands, transfers from hand to hand
- Writing, cutting, dressing

Vision and fine motor	Limit ages
Fixes and follows visually	3 months
Reaches for objects	6 months
Transfers	9 months
Pincer grip	12 months

Hearing, speech and language development

- Sound recognition, vocalisation
- Babbling
- Single words, understands simple requests
- Joining words, phrases
- Simple and complex conversation

Hearing, speech and language	Limit ages
Polysyllabic babble	7 months
Consonant babble	10 months
Saying 6 words with meaning	18 months
Joins words	2 years
3-word sentences	2.5 years

Social, emotional, behaviour development

- Smiling, socially responsive
- Separation anxiety
- Self-help skills, feeding, dressing, toileting
- Peer group relationships
- Symbolic play
- Social/communication behaviour

Social behaviour	Limit ages
Smiles	8 weeks
Fear of strangers	10 months
Feeds self/spoon	18 months
Symbolic play	2–2.5 years
Interactive play	3–3.5 years

Chapter 4: Developmental problems and the child with special needs

Table 4-1. Features that may suggest neurodevelopmental concerns by age

Prenatal	Positive family history, e.g. affected siblings or family members; ethnicity, e.g. Tay-Sachs disease in Jewish parents
	Antenatal screening tests, e.g. ultrasound including nuchal thickness and triple blood test for conditions such as Down syndrome, neural tube defects (spina bifida) and hydrocephalus. Amniocentesis for chromosomal disorders
Perinatal	Following birth asphyxia/neonatal encephalopathy
	Preterm infants with intraventricular haemorrhage/periventricular leucomalacia, post-haemorrhagic hydrocephalus
	Dysmorphic features
	Abnormal neurological behaviour - tone, feeding, movement, seizures, visual inattention
Infancy	Global developmental delay
	Delayed or asymmetric motor development
	Vision or hearing concerns by parent or after screening
	Neurocutaneous/dysmorphic features
Preschool	Speech and language delay
	Abnormal gait, clumsy motor skills
	Poor social communication skills
School age	Problems with balance and coordination
	Learning difficulties
	Attention control
	Hyperactivity
	Specific learning difficulties, e.g. dyslexia, dyspraxia
	Social communication difficulties
Any age	Acquired brain injury, e.g. after meningitis, head injury
	Loss of skills

Summary
Abnormal development

- Incorporates global and specific delay or disorder, learning difficulty, impairment and disability
- Varies in pattern of progression and severity
- Becomes more apparent with age.

Summary
Cerebral palsy

- has many causes. Only about 10% follow hypoxic-ischaemic encephalopathy
- usually presents in infancy with abnormal tone and posture, delayed motor milestones and feeding difficulties
- may be spastic, dyskinetic, ataxic or a mixed pattern.

Table 4-2. Conditions which cause abnormal development and learning difficulty

Prenatal	
Genetic	Chromosome/DNA disorders, e.g. Down syndrome, fragile X syndrome, chromosome microdeletions or duplications
	Cerebral dysgenesis, e.g. microcephaly, absent corpus callosum, hydrocephalus, neuronal migration disorder
Vascular	Occlusions, haemorrhage
Metabolic	Hypothyroidism, phenylketonuria
Teratogenic	Alcohol and drug abuse
Congenital infection	Rubella, cytomegalovirus, toxoplasmosis, HIV
Neurocutaneous syndromes	Tuberous sclerosis, neurofibromatosis
Perinatal	
Extreme prematurity	Intraventricular haemorrhage/periventricular leucomalacia
Birth asphyxia	Hypoxic-ischaemic encephalopathy
Metabolic	Symptomatic hypoglycaemia, hyperbilirubinaemia
Postnatal	
Infection	Meningitis, encephalitis
Anoxia	Suffocation, near drowning, seizures
Trauma	Head injury - accidental or non-accidental
Metabolic	Hypoglycaemia, inborn errors of metabolism
Vascular	Stroke
Other	
Unknown (about 25 %)	

Table 4-3. Investigations or assessment to consider for developmental delay

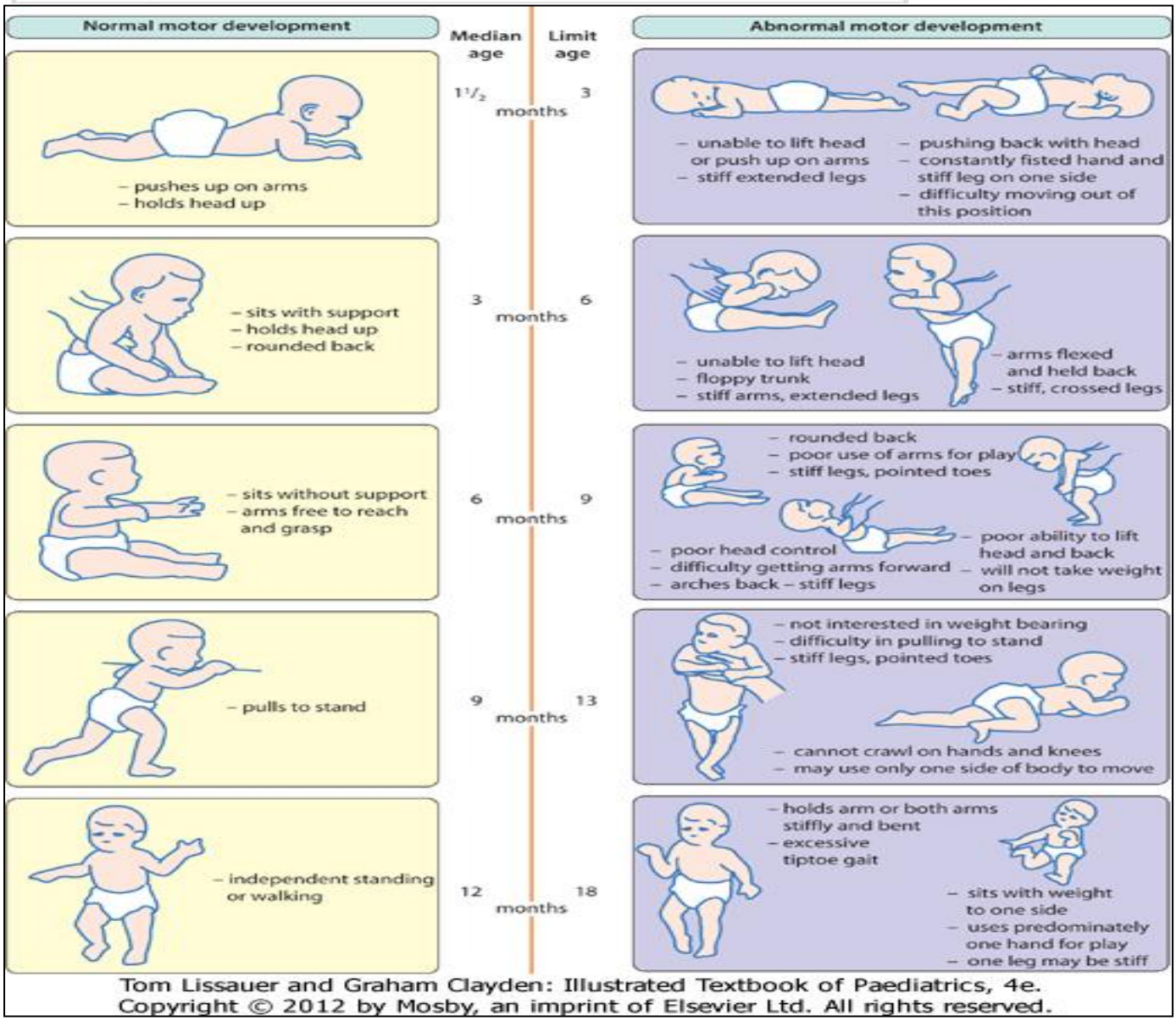
Cytogenetic	Chromosome karyotype[a]
	Fragile X analysis[a]
	DNA FISH analysis, e.g. for chromosome 7, 15, 22 deletions, CGH microarray (comparative genomic hybridisation), telomere screen
Metabolic	Thyroid function tests, liver function tests, bone chemistry, urea and electrolytes, plasma amino acids[a]
	Creatine kinase, blood lactate, VLCFA (very long chain fatty acids), ammonia, blood gases, white cell (lysosomal) enzymes, urine amino and organic acids, urine mucopolysaccharides (GAG) and oligosaccharide screen, urine reducing substances, lead levels, urate, ferritin, biotinidase
	Maternal amino acids for raised phenylalanine
Infection	Congenital infection screen
Imaging	Cranial ultrasound in newborn
	CT and MRI brain scans
	Skeletal survey, bone age
Neurophysiology	EEG (for seizures and can be specific for some progressive neurological disorders and syndromes)
	Nerve conduction studies, EMG, VEP (visual evoked potentials), ERG (electroretinogram)

Histopathology/ histochemistry	Nerve and muscle biopsy
Other	Hearing[a]
	Vision[a]
	Clinical genetics
	Cognitive assessment
	Therapy assessment - physiotherapy, occupational therapy and speech and language therapy
	Child psychiatry
	Dietician
	Nursery/school reports

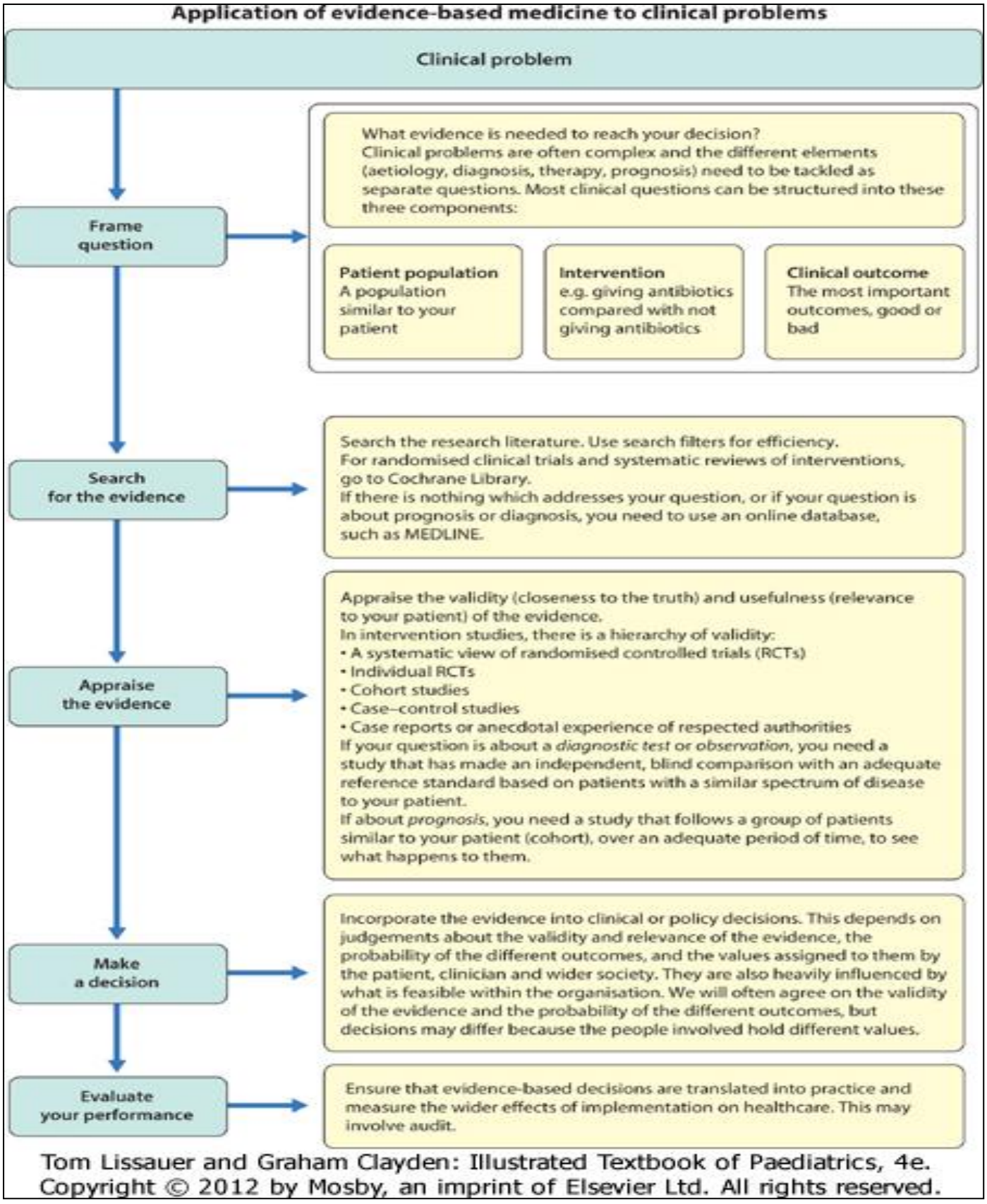
[a] basic screening test

Table 4-4. Gross Motor Function Classification System (GMFCS)

Level I	Walks without limitations
Level II	Walks with limitations
Level III	Walks using a handheld mobility device
Level IV	Self-mobility with limitations; may use powered mobility
Level V	Transported in a manual wheelchair



Chapter 5: Care of the sick child (EBM)



Example of evidence-based practice in solving a clinical problem – the management of acute otitis media

Clinical problem:
Should you treat a 3-year-old boy with otitis media with antibiotics?

Frame question

Population	Intervention	Outcomes
Children with acute otitis media	Antibiotics compared with none	Pain Hearing loss Adverse drug side-effects Other complications

Search for the evidence

Cochrane Library – 22 meta-analyses, one corresponding best to this child

Appraise the evidence

Antibiotics have no effect on pain in the first 24 hours, but a 30% reduction in pain at 2–7 days.
There is a possible reduction in hearing loss, perforation of the drum and contralateral otitis media but this does not reach statistical significance.
There is a near doubling in the chance of diarrhoea, rashes and abdominal pain.
However:
- for the risk of severe complications of the disease (mastoiditis, meningitis) or of antibiotic therapy, the sample size was too small
- potential costs to society in antibiotic resistance and finance have not been evaluated.

Make a decision

You explain to the parent that antibiotics:
- would reduce the risk of pain lasting 2–7 days but about 17 children need to be treated for one to benefit, and this would not reduce the risk of hearing loss
- would increase the risk of minor side-effects.

The decision whether or not to treat depends on the parents' values about pain and adverse side-effects. One approach would be to give this information and a prescription for antibiotics to parents and ask them to wait 2–3 days and use their prescription only if the child is still unwell.

2. Clear evidence, but need to balance benefits and harms

Antibiotic treatment for children with otitis media

As shown in Figure 5.9, there is a balance of risk and benefits.

3. No clear evidence

Bulk-forming laxatives for constipation

Bulk-forming laxatives, such as methylcellulose or ispaghula husk, are used in children with constipation. However, this is not based on clear evidence. There are no systematic reviews and no randomised controlled studies of these agents in children.

Some possible reasons for the lack of evidence on the use of these laxatives in this common condition are:

- - constipation is not a life-threatening disorder
- - the causes are multifactorial and the disease mechanism is not clearly defined
- - there is a belief that there are likely to be few side-effects to the use of bulk-forming laxatives and clinicians are prepared to prescribe them without clear evidence
- - there is limited support for studies from the pharmaceutical industry
- - the research agenda is not driven by such clinical problems.

Box 5.4 Examples of the range of evidence available in paediatrics
1. Clear evidence of benefit

Surfactant therapy in pre-term infants

The meta-analysis (see Fig. 10.12) from a Cochrane systematic review shows that mortality is reduced by 40% in preterm infants with respiratory distress syndrome (RDS) treated with surfactant compared with placebo.

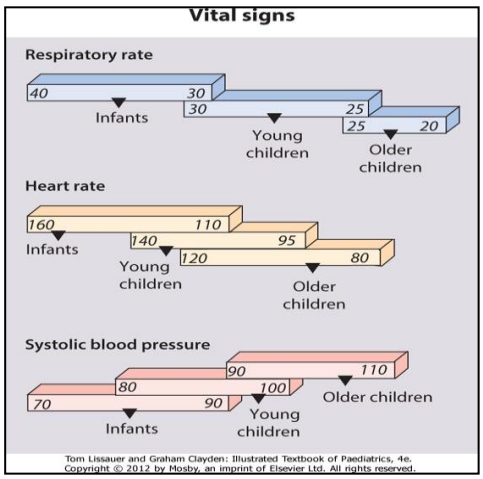
This evidence was rapidly produced and introduced into practice as:

- - Respiratory distress syndrome is a common cause of death and morbidity in a neonatal intensive care unit
- - There is a clearly understood disease mechanism for respiratory distress syndrome, i.e. surfactant deficiency
- - The effect of surfactant treatment was immediately obvious at the cot-side - ventilator settings usually have to be reduced shortly after administration
- - Potential benefits and side-effects could be clearly defined and identified
- - Neonatologists are a relatively small group of doctors who meet regularly - national and international studies could be organised and their results quickly disseminated
- - There was financial support and involvement from the pharmaceutical industry.

Summary
Evidence-based paediatrics

- requires clinical problems to be framed into questions, to search the literature and then appraise the evidence in order to make a decision
- is less well developed than in adult medicine
- should be adopted whenever possible; however, clinical decisions are complex and the evidence base usually informs rather than determines clinical decision-making.

Chapter 6: pediatric emergences



• Doctors should be able to provide life support for children of all ages, from newborn to adolescents.

Summary
Regarding the seriously ill child

- Prevention of cardiopulmonary arrest is by early recognition and treatment of respiratory distress, respiratory or circulatory failure.

Assessment of the seriously ill child

The rapid clinical assessment:
ABCDE
Should take < 1 min

Airway and Breathing
Look, listen and feel for:
Airway obstruction or respiratory distress
Work of breathing (respiratory effort)
Respiratory rate
Stridor, wheeze
Auscultation for air entry
Cyanosis

Circulation
Feel and assess:
Heart rate
Pulse volume
Capillary refill time (Fig 6.3)
Blood pressure

Disability
Observe and note:
Level of consciousness (Box 6.1)
Posture – hypotonia, decorticate, decerebrate
Pupil size and reactivity

Exposure

→

Resuscitation (if necessary)

Includes Basic/Advanced life support
Consider:
Jaw and neck positioning
Oxygen
Suction and foreign body removal
Supporting breathing
Chest compression
Monitoring pulse oximetry and heart rate

↓

Secondary assessment

History from:
- parents
- witnesses
- general practitioner
- paramedical staff
- police

Examination including:
- evidence of trauma
- rash, e.g. meningococcal
- smell, e.g. ketones, alcohol
- scars, e.g. underlying congenital heart disease
- MedicAlert bracelet

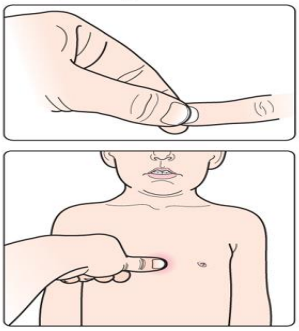
Investigations
- blood glucose

↓

Other emergency interventions

Tom Lissauer and Graham Clayden: Illustrated Textbook of Paediatrics, 4e.

Capillary refill time



Press on the skin of the sternum or a digit at the level of the heart
Apply blanching pressure for 5 seconds
Measure time for blush to return
Prolonged capillary refill if >2 seconds

- Capillary refill time is affected by body exposure to a cold environment.

Box 6.1 AVPU rapid assessment of level of consciousness - more detailed evaluation is with the Glasgow Coma Scale (see Table 6.2)

A	ALERT
V	Responds to VOICE
P	Responds to PAIN
U	UNRESPONSIVE

A score of P means that the child's airway is at risk and will need to be maintained by a manoeuvre or adjunct.

Presentation and causes of serious illness in children

Presentation	Cause	Examples
Shock	Hypovolaemia	Dehydration – gastroenteritis Diabetic ketoacidosis Blood loss – trauma
	Maldistribution of fluid	Septicaemia Anaphylaxis
	Cardiogenic	Arrhythmias Heart failure
Respiratory distress	Upper airway obstruction (stridor)	Croup/epiglottitis Foreign body Congenital malformations Trauma
	Lower airway disorders	Asthma Bronchiolitis Pneumonia Pneumothorax
The drowsy or unconscious or seizing child	Post-ictal Status epilepticus	
	Infection	Meningitis/encephalitis
	Metabolic	Diabetic ketoacidosis, hypoglycaemia, electrolyte disturbances (calcium, magnesium, sodium), inborn error of metabolism
	Head injury	Trauma/non-accidental injury
	Drug/poison ingestion	
	Intracranial haemorrhage	
Surgical emergencies	Acute abdomen	Appendicitis Peritonitis
	Intestinal obstruction	Intussusception Malrotation Bowel atresia/stenosis

Basic life support

(Trained resuscitator, no equipment)

SAFE approach → Shout for help
Approach with care
Free from danger
Evaluate **ABC**

Check responsiveness:
Ask 'Are you all right?'
Stimulate gently
Do not shake infants or suspected cervical spine injury

↓ **No response**

Open airway:
- Head tilt, chin lift
- Jaw thrust (if unsuccessful)

→ **Airway**
Airway opening using head tilt/chin lift manoeuvre

Chin lift in infants
- Head in **neutral** position
- Avoid overextension
- Remove secretions/foreign body under direct vision

Chin lift in children
Head in 'sniffing' position

Jaw thrust
Two fingers of each hand behind each side of the mandible and push the jaw forward

↓ **No breathing**

Check breathing for max 10 s:
- Look – for chest movement
- Listen – for breath sounds
- Feel – for air movement

Breathe
Remove any obvious obstruction
Give 5 initial rescue breaths

→ **Breathing**
Infant: Mouth over infant's nose and mouth
Child: Pinch nose, mouth to mouth
The chest should rise with each breath. Blow for 1–1.5 seconds

Assess 'signs of life' - movements, coughing, normal breathing
Check pulse for max 10 s:
>1 year old – carotid, femoral
<1 year old – brachial, femoral

↓ **No 'signs of life' (unless definite pulse >60/min)**

Compress chest
15 chest compressions: 2 breaths
Rate 100–120 compressions/min
Compression: ventilation ratio for all children:
two rescuers (or lone trained resuscitator) – 15:2
lone rescuer (not trained) – 30:2

→ **Circulation**
Optimal position for chest compression

(a) **Infant.** Two thumbs on lower third of sternum with hands round the thorax (needs two rescuers). If alone – compress sternum with tips of two fingers.
(b) **Small child.** Heel of one hand over lower third of sternum.
(c) **Large child.** Both hands over lower third of sternum. Depress the sternum by at least one-third of the depth of the chest

Push 'hard and fast'

What should an untrained bystander do?
Perform chest compressions or expired air ventilation (mouth-to-mouth) – it's better than doing nothing

Advanced life support
(Health professional with equipment)

Unresponsive?
Not breathing or only occasional gasps?

→ **Call resuscitation team**
(1 min CPR first, if alone)

Airway and Breathing Airway
– see basic life support
Breathing – 5 initial rescue breaths
Use positive pressure ventilation, preferably bag and mask. If required and skilled operator present, advanced airway – intubate and ventilate or laryngeal mask
Give high concentration O_2

→ **Formula for endotracheal tube size by age in whole years**
Internal diameter (mm) = (age/4) + 4
Length for oral tube (cm) = (age/2) + 12
Length for nasal tube (cm) = (age/2) + 15

Circulation
15 chest compressions: 2 breaths
Compression rate 100–120/min (continuously if intubated)
Ventilation rate 10–12/min
Establish intravenous access, if delay use intraosseous route

→ **Technique to establish intraosseous infusion in the tibia**
- 18-gauge trochar with needle
- Anterior surface, 2–3 cm below tibial tuberosity

Attach defibrillator/monitor
Minimise interruption

Assess rhythm

Shockable
Ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT)

→ **1 Shock**
4J/kg

→ Immediately resume **CPR for 2 min**
Minimise interruptions

→ **Give adrenaline (epinephrine) every 3–5 min**
i.e. after 3rd shock and then after alternate cycles (10 micrograms/kg IV or IO, i.e. 0.1 ml/kg of 1 in 10000 solution), otherwise 100 micrograms/kg via tracheal tube)
Give amiodarone 5 mg/kg after 3rd and 5th shock

Return of spontaneous circulation

→ **Immediate post-cardiac arrest treatment**
- Use ABCDE approach
- Controlled oxygenation and ventilation
- Investigations
- Treat precipitating cause
- Temperature control
- Therapeutic hypothermia?

Non-shockable
Pulseless electrical activity (PEA) or asystole

→ Immediately resume **CPR for 2 min**
Minimise interruptions

→ **Give adrenaline (epinephrine) every 3–5 min**
i.e. every other cycle

During CPR
- Ensure high-quality CPR: rate, depth, recoil
- Plan actions before interrupting CPR
- Give oxygen
- Vascular access (intravenous, intrasseous)
- Give adrenaline (epinephrine) every 3–5 min
- Consider advanced airway and capnography (end-tidal CO_2 monitoring)
- Continuous chest compressions when advanced airway in place
- Correct reversible causes

Reversible causes
- Hypoxia
- Hypovolaemia
- Hypo-/hyperkalaemia/metabolic
- Hypothermia
- Tension pneumothorax
- Toxins
- Tamponade – cardiac
- Thromboembolism

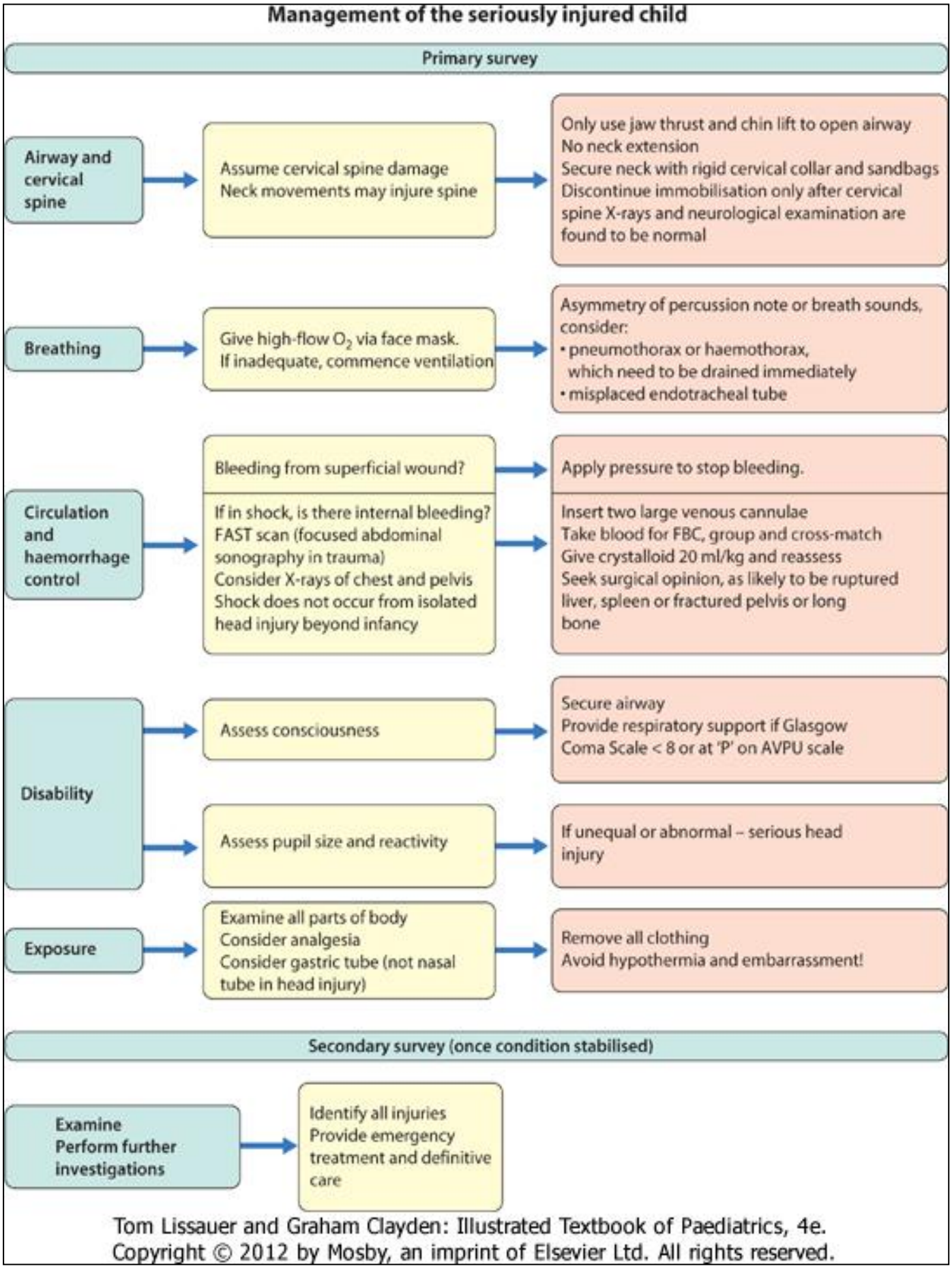


Table 6-1. Fluid intake at different ages

Body weight	Fluid requirement/24 h	Volume/kg per hour (approximate)
First 10 kg	100 ml/kg	4 ml/kg
Second 10 kg	50 ml/kg	2 ml/kg
Subsequent kg	20 ml/kg	1 ml/kg
Examples of calculations		
Infant (7 kg)	700 ml	28 ml/h
Child (18 kg)	1000 + 400 = 1400 ml	40 + 16 = 56 ml/h
Adolescent (42 kg)	1000 + 500 + 440 = 1940 ml	40 + 20 + 22 = 82 ml/h

Box 6.2 Clinical signs of shock

Early (compensated)	Late (decompensated)
Tachypnoea	Acidotic (Kussmaul) breathing
Tachycardia	Bradycardia
Decreased skin turgor	Confusion/depressed cerebral state
Sunken eyes and fontanelle	Blue peripheries
Delayed capillary refill (>2 s)	Absent urine output
Mottled, pale, cold skin	Hypotension
Core-peripheral temperature gap (>4°C)	
Decreased urinary output	

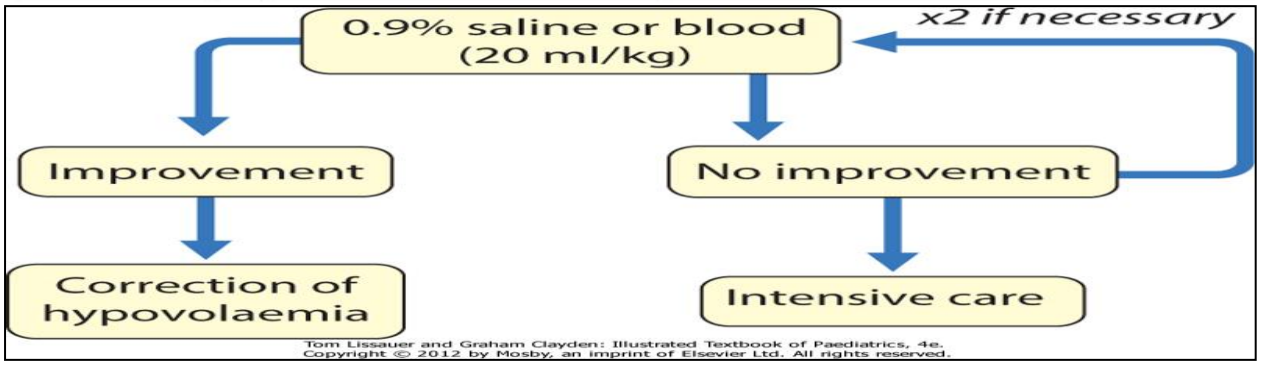


Figure 6.8 Initial fluid resuscitation in shock.

Box 6.3 Clinical features of septicaemia

History	Examination
Fever	Fever
Poor feeding	Tachycardia, tachypnoea, low blood pressure
Miserable, irritable, lethargy	Purpuric rash (meningococcal septicaemia) (Fig. 6.9).
History of focal infection, e.g. meningitis, osteomyelitis, gastroenteritis, cellulitis	Shock
Predisposing conditions, e.g. sickle cell disease, immunodeficiency	Multi-organ failure

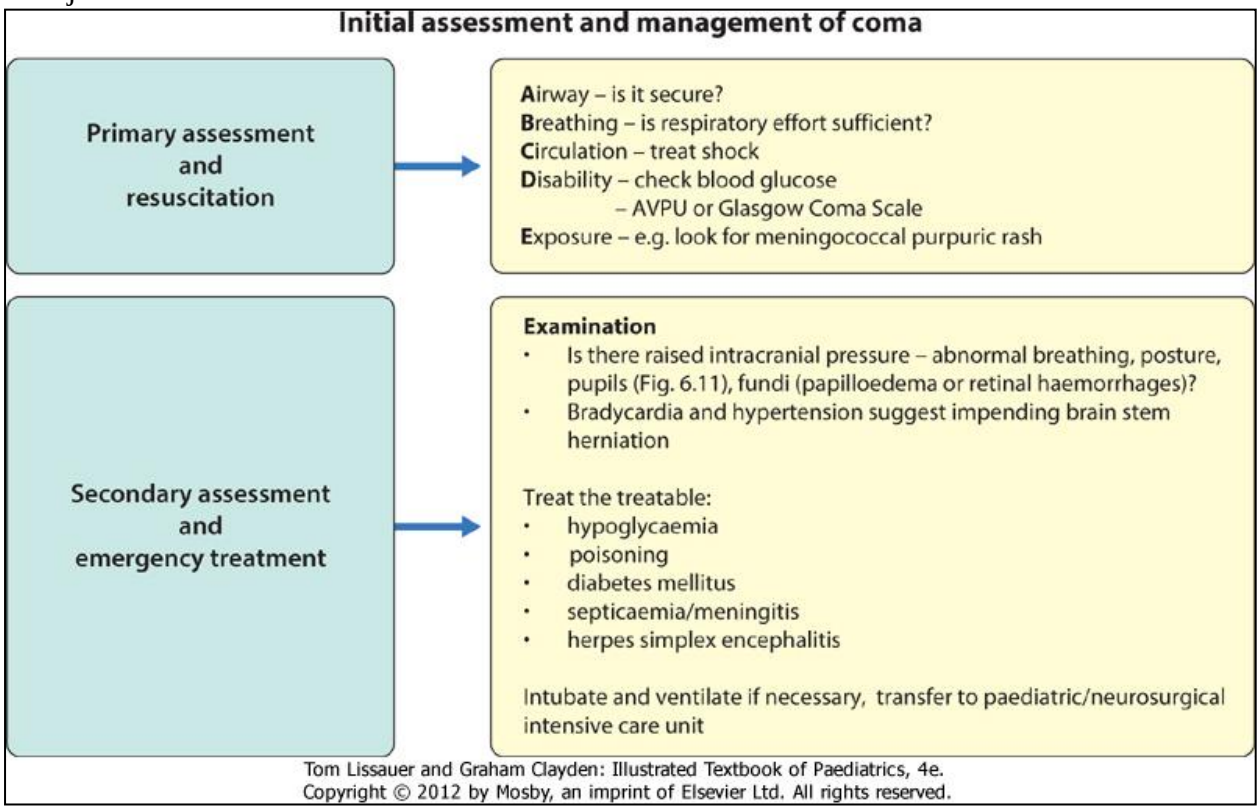
Summary
Septicaemia

- The most common cause of septic shock in children is meningococcal disease
- May occur without meningitis
- Early antibiotic therapy and fluid resuscitation are life-saving
- May need admission to paediatric intensive care for multi-organ failure.

Table 6-2. Glasgow Coma Scale, incorporating Children's Coma Scale

	Glasgow Coma Scale (4-15 years) Response	Children's Coma Scale (<4 years) Response	Score
Eyes	Open spontaneously	Open spontaneously	4
	Verbal command	React to speech	3
	Pain	React to pain	2
	No response	No response	1
Best motor response			
Verbal command	Obeys	Spontaneous or obeys verbal command	6
Painful stimulus	Localises pain	Localises pain	5
	Withdraws	Withdraws	4
	Abnormal flexion	Abnormal flexion (decorticate posture)	3
	Extension	Abnormal extension (decerebrate posture)	2
	No response	No response	1
Best verbal response	Oriented and converses	Smiles, orientated to sounds, follows objects, interacts	5
	Disoriented and converses	Fewer than usual words, spontaneous irritable cry	4
	Inappropriate words	Cries only to pain	3
	Incomprehensible sounds	Moans to pain	2
	No response	No response to pain	1

A score < 8 out of 15 means that the child's airway is at risk and will need to be maintained by a maneuver or adjunct



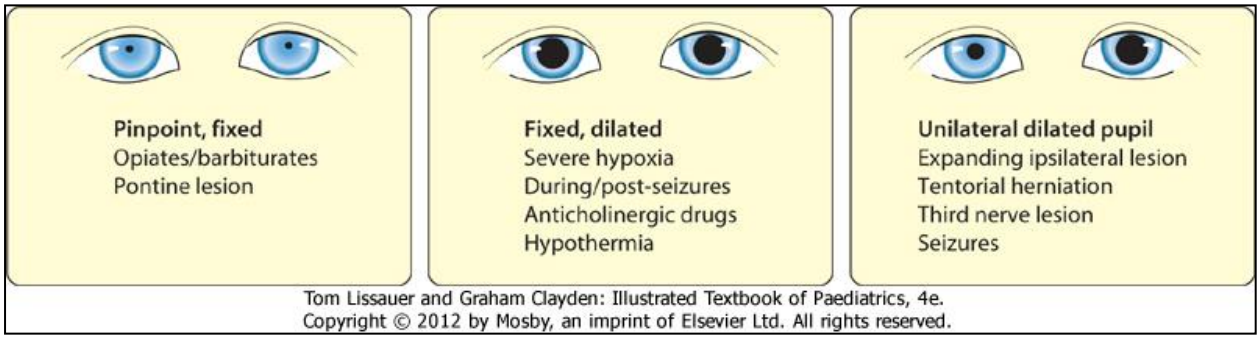
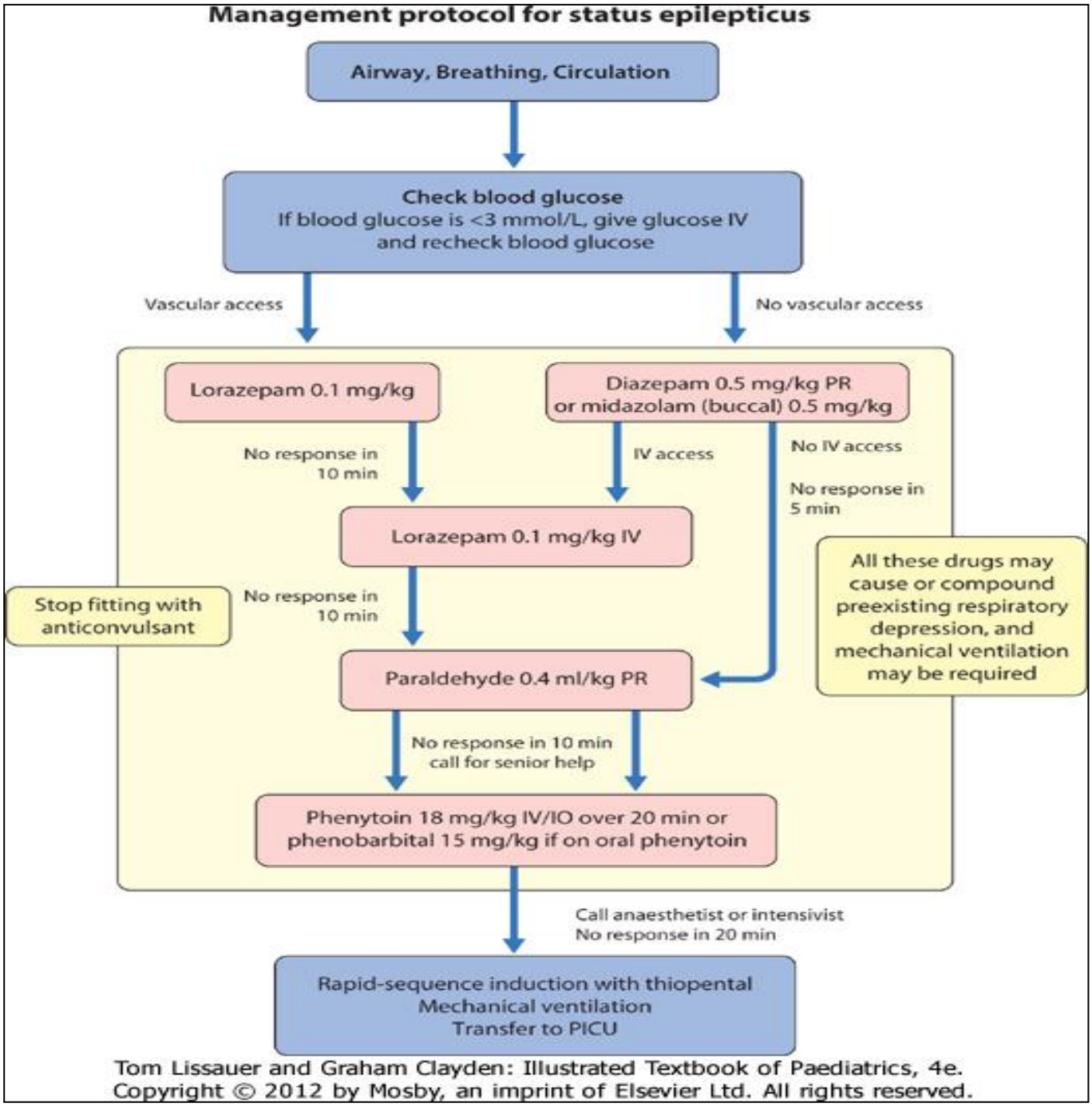


Figure 6.11 Pupillary signs in coma.

Table 6-3. Causes, history and examination and investigation of coma

Cause	History and examination	Diagnostic investigations
Infection Meningitis or meningoencephalitis	Fever Irritability, lethargy, drowsiness Poor feeding, vomiting Rash, e.g. meningococcal purpura Seizures Neck stiffness and pain; bulging fontanelle Overseas travel	Full blood count Culture of blood, urine, infected sites, CSF (unless contraindicated) for bacteria and viruses Acute-phase reactant Rapid bacterial antigen/PCR tests for organisms
Status epilepticus or post-ictal	Past history of seizures Neurocutaneous lesions on the skin Developmental delay Ongoing seizure activity, e.g. abnormal eye movements Focal neurological signs	Blood glucose Electrolytes - sodium, potassium, calcium, magnesium Drug levels if on anticonvulsants EEG CT scan
Trauma - accidental/non-accidental	History of road traffic accident, fall, etc. Bruising, haemorrhage Fractures - cervical spine, etc. Focal neurology Retinal haemorrhages	Radiological - plain X-rays or CT/MRI scans
Intracranial tumour or haemorrhage/infarct/abscess	Symptoms or signs of raised intracranial pressure Focal neurological signs, e.g. squint	Cranial CT/MRI scan Haemorrhage - coagulation screen, screen for procoagulant disorders (protein C/S deficiency)
Metabolic		
1. Diabetes mellitus	Previously diagnosed diabetes mellitus Diabetic ketoacidosis	Blood glucose, plasma electrolytes Urine for glucose and ketones Blood gas analysis
2. Hypoglycaemia	Any acutely ill child Known diabetes mellitus Sudden onset of coma	Low blood glucose
3. Inborn errors of metabolism	Previous history of loss of consciousness Sudden collapse Consanguinity, death or illness of siblings Developmental delay Hepatomegaly	Blood glucose Blood gas analysis Blood ammonia, lactate Urine amino and organic acids Plasma amino acids
4. Hepatic failure	Jaundice Abnormal bleeding	Abnormal liver function tests Prolonged prothrombin time
5. Acute renal failure	Oliguria, hypertension	Abnormal creatinine

Poisoning	Accidental - poison usually identified Deliberate - tablets may be found, also illicit drugs and alcohol	Toxicology screen Plasma level for paracetamol and salicylates
Shock	Septicaemia Dehydration Cardiac failure	Full blood count and cultures Urea, electrolytes, blood gas
Hypertension	Symptoms and signs of raised intracranial pressure Fundoscopy - hypertensive changes	Left ventricular hypertrophy on ECG or echocardiography Creatinine and electrolytes
Respiratory failure	Respiratory failure	Chest X-ray Arterial blood gas - hypoxia, hypercarbia



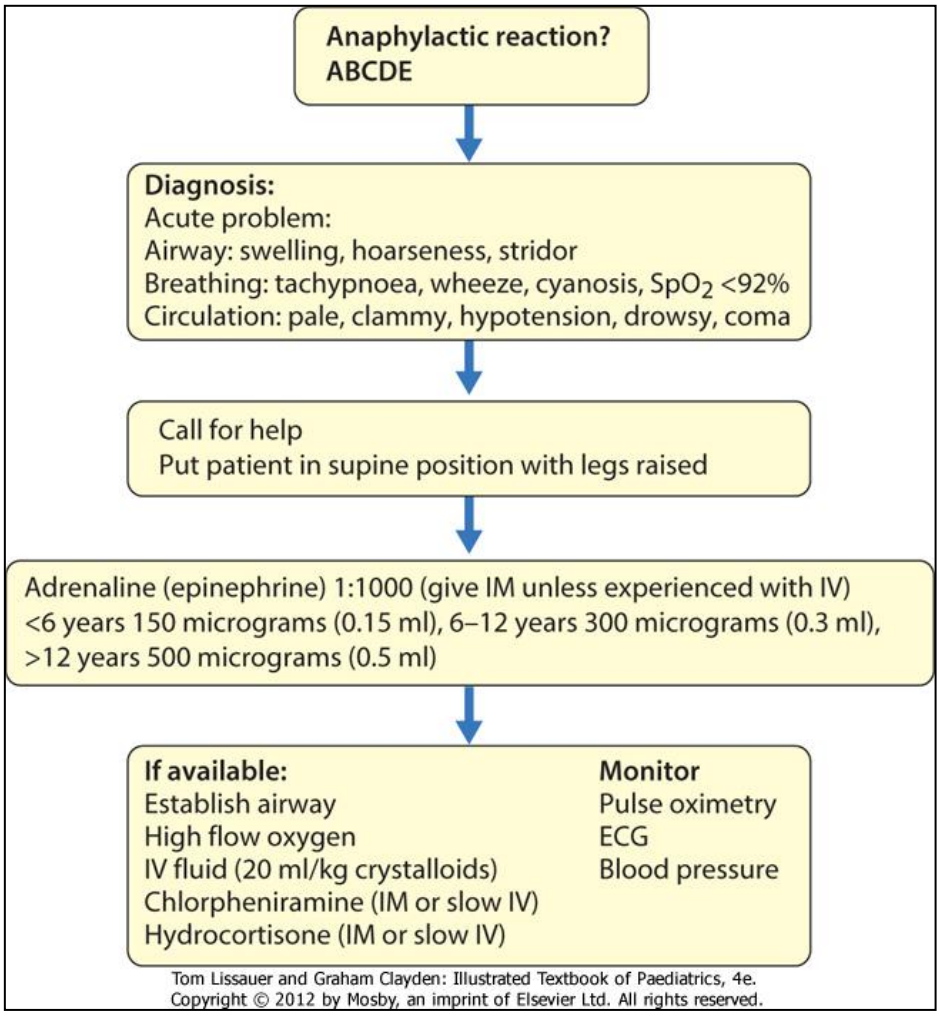


Figure 6.13 Emergency treatment of anaphylaxis.

Box 6.4 Causes and investigations to be considered in apparent life-threatening events

Causes

- Infections - respiratory syncytial virus (RSV), pertussis
- Seizures
- Gastro-oesophageal reflux (present in one-third of normal infants)
- Upper airways obstruction - natural or imposed
- No cause identified

Uncommon causes

- Cardiac arrhythmia
- Breath-holding
- Anaemia
- Heavy wrapping/heat stress
- Central hypoventilation syndrome
- Cyanotic spells from intrapulmonary shunting

Investigations to be considered

- Blood glucose (as soon as possible)
- Blood gas (as soon as possible)
- Oxygen saturation monitoring
- Cardiorespiratory monitoring
- EEG
- Oesophageal pH monitoring
- Barium swallow
- Full blood count
- Urea and electrolytes, liver function tests
- Lactate
- Urine (collect and freeze first sample)
  - - metabolic studies
  - - microscopy and culture
  - - toxicology
- ECG - for QT_c conduction pathway abnormality
- Chest X-ray
- Lumbar puncture.

Chapter 8: Genetics

Box 8.1 Characteristic clinical manifestations of Down syndrome

Typical craniofacial appearance

- Round face and flat nasal bridge
- Upslanted palpebral fissures
- Epicanthic folds (a fold of skin running across the inner edge of the palpebral fissure)
- Brushfield spots in iris (pigmented spots)
- Small mouth and protruding tongue
- Small ears
- Flat occiput and third fontanelle

Other anomalies

- Short neck
- Single palmar creases, incurved fifth finger and wide 'sandal' gap between toes
- Hypotonia
- Congenital heart defects (40%)
- Duodenal atresia
- Hirschsprung disease

Later medical problems

- Delayed motor milestones
- Moderate to severe learning difficulties
- Small stature
- Increased susceptibility to infections
- Hearing impairment from secretory otitis media
- Visual impairment from cataracts, squints, myopia
- Increased risk of leukaemia and solid tumours
- Risk of atlanto-axial instability
- Increased risk of hypothyroidism and coeliac disease
- Epilepsy
- Alzheimer's disease.

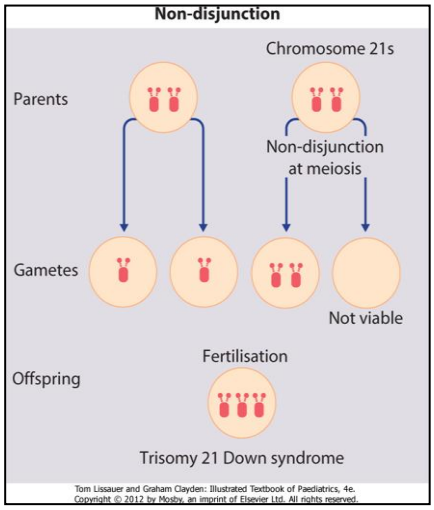


Figure 8.3 Non-disjunction Down syndrome.

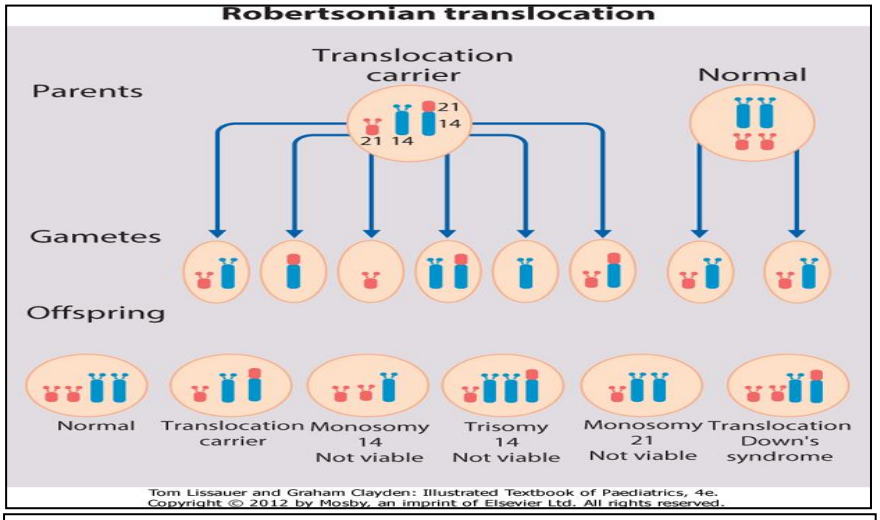


Figure 8.4 Translocation Down syndrome. There is a Robertsonian translocation involving chromosomes 21 and 14, which has been inherited from a parent.

Summary
Down syndrome (trisomy 21)

- Natural incidence ~1.5 per 1000 infants
- Cytogenetics - non-disjunction (most common, related to maternal age), translocation (one parent may carry a balanced translocation) or mosaicism (rare)
- Presentation - antenatal screening, prenatal diagnosis or clinical presentation; confirmed on chromosome analysis
- Immediate medical complications - increased risk of duodenal atresia, congenital heart disease
- Clinical manifestations (see Box 8.1).

Box 8.2 Clinical features of Edwards syndrome (trisomy 18)

- Low birthweight
- Prominent occiput
- Small mouth and chin
- Short sternum
- Flexed, overlapping fingers (Fig. 8.5)
- 'Rocker-bottom' feet
- Cardiac and renal malformations.

Box 8.3 Clinical features of Patau syndrome (trisomy 13)

- Structural defect of brain
- Scalp defects
- Small eyes (microphthalmia) and other eye defects
- Cleft lip and palate
- Polydactyly
- Cardiac and renal malformations.

Box 8.4 Clinical features of Turner syndrome

- Lymphoedema of hands and feet in neonate, which may persist
- Spoon-shaped nails
- Short stature - a cardinal feature
- Neck webbing or thick neck
- Wide carrying angle (cubitus valgus)
- Widely spaced nipples
- Congenital heart defects (particularly coarctation of the aorta)
- Delayed puberty
- Ovarian dysgenesis resulting in infertility, although pregnancy may be possible with in vitro fertilisation (IVF) using donated ova
- Hypothyroidism
- Renal anomalies
- Pigmented moles
- Recurrent otitis media
- Normal intellectual function in most.

Box 8.5 Clinical features of Klinefelter syndrome

- Infertility - most common presentation
- Hypogonadism with small testes
- Pubertal development may appear normal (some males benefit from testosterone therapy)
- Gynaecomastia in adolescence
- Tall stature
- Intelligence usually in the normal range, but some have educational and psychological problems.

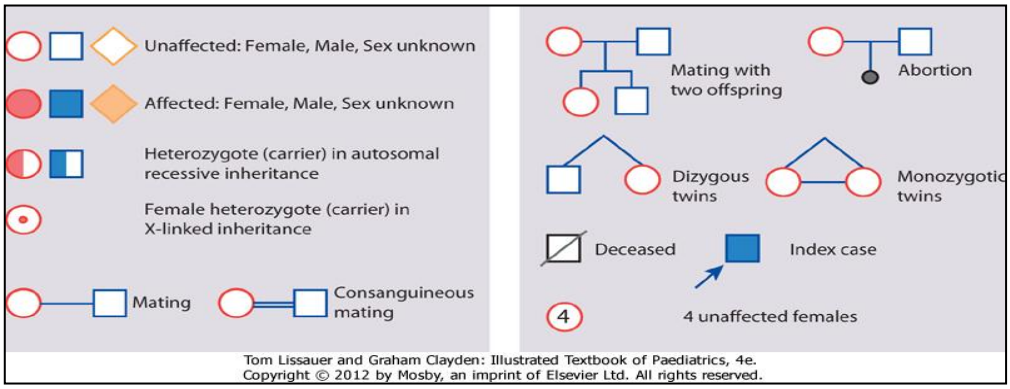


Figure 8.8 Examples of pedigree symbols.

Autosomal dominant inheritance

Box 8.6 Examples of autosomal dominant

- Achondroplasia
- Ehlers-Danlos syndrome
- Familial hypercholesterolaemia
- Huntington disease
- Marfan syndrome
- Myotonic dystrophy
- Neurofibromatosis
- Noonan syndrome
- Osteogenesis imperfecta
- Otosclerosis
- Polyposis coli
- Tuberous sclerosis.

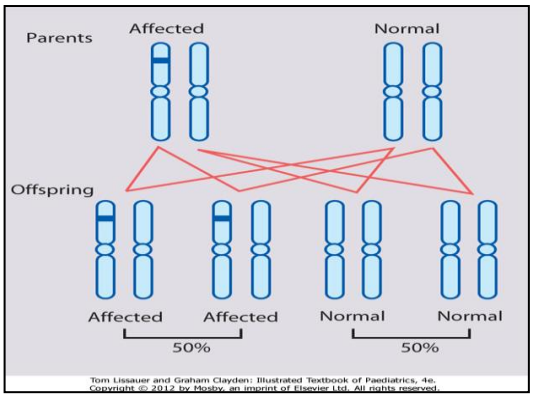


Figure 8.9a Autosomal dominant inheritance.

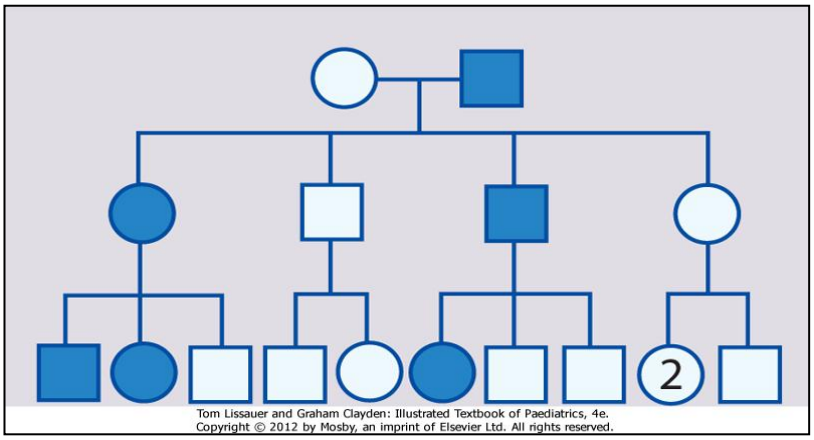


Figure 8.9b typical pedigree of an autosomal dominant disorder

Summary
Autosomal dominant inheritance

- Most common mode of Mendelian inheritance
- Affected individual carries the abnormal gene on one of a pair of autosomes
- 1 in 2 chance of inheriting the abnormal gene from affected parent, but there may be variation in expression, non-penetrance, no family history (new mutation, parental mosaicism, non-paternity) or homozygosity (rare).

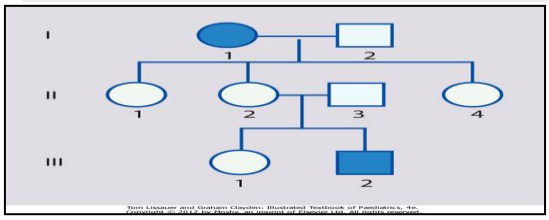


Figure 8.10 Example of non-penetrance. I1 and III2 have otosclerosis. II2 has normal hearing but must have the gene (a new mutation event is most unlikely to arise independently for a second time in the family). The gene is non-penetrant in II2.

Autosomal recessive inheritance

Box 8.7 Examples of autosomal recessive disorders

- Congenital adrenal hyperplasia
- Cystic fibrosis
- Friedreich ataxia
- Galactosaemia
- Glycogen storage diseases
- Hurler syndrome
- Oculocutaneous albinism
- Phenylketonuria
- Sickle cell disease
- Tay-Sachs disease
- Thalassaemia
- Werdnig-Hoffmann disease (SMA I).

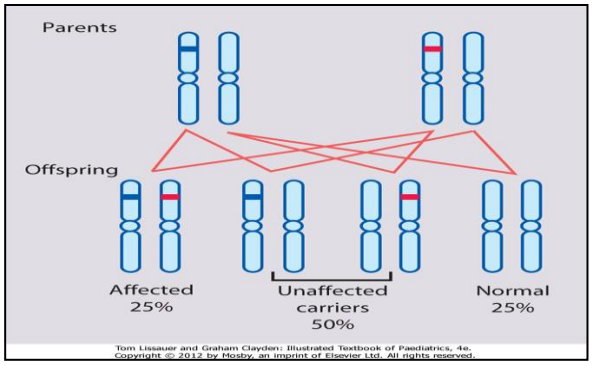


Figure 8.11a Autosomal recessive inheritance

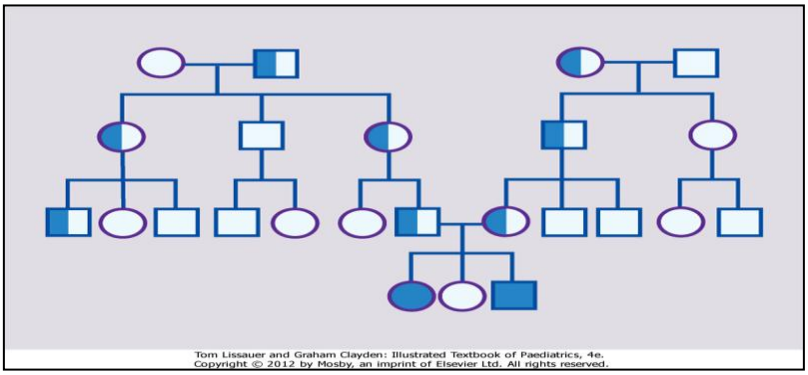


Figure 8.11b Pedigree to show autosomal recessive inheritance.

Summary
Autosomal recessive inheritance

- Affected individuals are homozygous for the abnormal gene; each unaffected parent will be a heterozygous carrier
- Two carrier parents have a 1 in 4 risk of having an affected child
- Risk of these disorders is increased by consanguinity and within specific populations
- Autosomal recessive disorders often affect metabolic pathways, whereas autosomal dominant disorders often affect structural proteins.

X-linked recessive inheritance

Box 8.8 Examples of X-linked recessive disorders

- Colour blindness (red-green)
- Duchenne and Becker muscular dystrophies
- Fragile X syndrome
- Glucose-6-phosphate dehydrogenase (G6PD) deficiency
- Haemophilia A and B
- Hunter syndrome (mucopolysaccharidosis II).

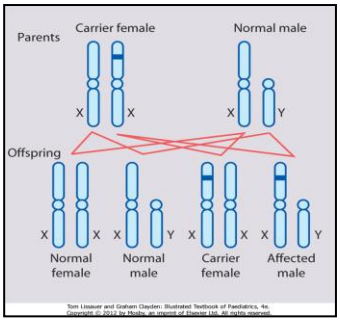


Figure 8.12a X-linked recessive inheritance.

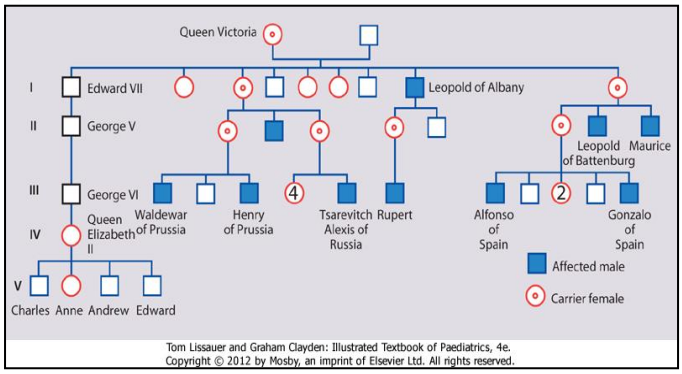


Figure 8.12b Typical pedigree for X-linked recessive inheritance, showing Queen Victoria, a carrier for haemophilia A, and her family. It shows affected males in several generations, related through females, and that affected males do not have affected sons (contrast with autosomal dominant inheritance).

Summary
X-linked recessive inheritance

- Males are affected; females can be carriers but are usually healthy or have mild disease
- Family history may be negative - new mutations and gonadal mosaicism
- Identifying female carriers is important to be able to provide genetic counselling.

Box 8.9 Clinical findings in males in fragile X syndrome

- Moderate-severe learning difficulty (IQ 20-80, mean 50)
- Macrocephaly
- Macro-orchidism - postpubertal
- Characteristic facies - long face, large everted ears, prominent mandible and broad forehead, most evident in affected adults
- Other features - mitral valve prolapse, joint laxity, scoliosis, autism, hyperactivity.

• Fragile X syndrome is the commonest familial form of learning difficulties and the second most common genetic cause of severe learning difficulties after Down syndrome.

Box 8.10 Conditions often associated with multifactorial (polygenic, complex) inheritance

Congenital malformations
- Neural tube defects (anencephaly and spina bifida)
- Congenital heart disease
- Cleft lip and palate
- Pyloric stenosis
- Congenital dislocation of the hip
- Talipes equinovarus
- Hypospadias

Childhood
- Atopy (especially asthma and eczema)
- Epilepsy
- Diabetes mellitus type 1 (insulin-dependent diabetes)

Adult life
- Atherosclerosis and coronary artery disease
- Diabetes mellitus type 2
- Alzheimer's disease
- Malignancy (especially the common cancers, e.g. breast and colorectal cancer)
- Hypertension
- Cerebrovascular disease (especially stroke).

Case History 8.1 Syndrome diagnosis and genetic counselling

Sean, the second child of healthy parents, was born at term by emergency caesarean section for fetal distress. The pregnancy had been uneventful and no abnormalities were detected on antenatal ultrasound scan. He developed respiratory distress and investigation for a cardiac murmur revealed an interrupted aortic arch and ventricular septal defect that required surgical correction in the neonatal period.

The parents asked about recurrence risk for congenital heart disease and were referred to the genetic clinic. At that time, Sean was thriving and early developmental progress appeared normal. On examination, there were minor dysmorphic features, including a short philtrum, thin upper lip and prominent ears (Fig. 8.20). There was no family history of congenital heart disease or other significant problems and no abnormalities were detected on examination of the parents.

Because of an association between outflow tract abnormalities of the heart and deletions of chromosome 22, cytogenetic analysis was performed using fluorescent in situ hybridisation (FISH). A submicroscopic deletion of the long arm of one chromosome 22 (band 22q11) was detected. Other features of DiGeorge syndrome (hypocalcaemia and T-cell deficiency), which occurs with the same chromosome deletion, were excluded by appropriate tests but could have been important in Sean's medical management.

Parental chromosome analysis showed no deletion at chromosome 22q11 in either parent, indicating a low recurrence risk for future pregnancies since gonadal mosaicism for this deletion is very rare. The older sibling was also normal on testing. Because the parents had normal karyotypes, their own brothers and sisters did not need to be offered tests.

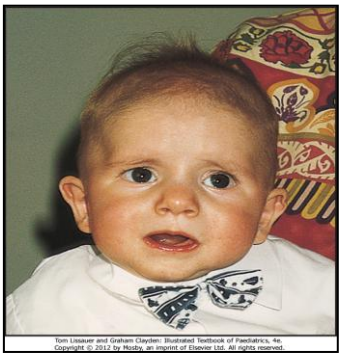


Figure 8.20 Sean's facial appearance showing the short philtrum (vertical groove in the upper lip), thin upper lip and prominent ears.

Identification of a 22q11 deletion indicated that other associated problems were likely. Subsequently, Sean required assessment by a multidisciplinary child development team (for developmental delay), that led to educational statementing and recommendation for appropriate placement in a school for children with special educational needs (learning difficulty), input from a clinical psychologist when behavioural problems appeared (ritualistic behaviour and obsessional tendencies), input from speech therapist and plastic surgeon (indistinct speech due to velopharyngeal incompetence) and audiology review (conductive hearing loss due to recurrent otitis media).

The impact of the diagnosis and its implications was considerable for the family and the parents needed support from a variety of professionals while coming to terms with the various problems as they became apparent. Written information and details of the 22q11 support group were given to the parents. Medical care was coordinated by the paediatrician.

There was the additional worry for the family about a subsequent pregnancy. Fetal echocardiography showed no evidence of congenital heart disease, but invasive tests for cytogenetic analysis were declined because of the low recurrence risk. The baby was born unaffected, with chromosome studies performed on a cord blood sample revealing no abnormality.

Table 8-2. Genetic investigations

Investigation	Application
Cytogenetic analysis - karyotype	Chromosomes stained and visualised under a microscope
	Detects alterations in chromosome number and structural rearrangements; this method is being replaced by molecular methods such as CGH.
Molecular cytogenetic analysis - FISH (fluorescent in situ hybridisation)	Fluorescent-labelled DNA probes to detect the presence, number and chromosomal location of specific chromosomal sequences
	Useful for microdeletion syndromes
Microarray comparative genomic hybridisation (aCGH)	Detects chromosomal imbalances using thousands of DNA probes to investigate a whole genome with much greater sensitivity than cytogenetic methods
DNA analysis	Polymerase chain reaction (PCR) to amplify the DNA and determine the sequence of the relevant gene
High throughput DNA sequencing	Rapid sequencing of whole genomes or many loci within the genome
Linkage disequilibrium and genome-wide association studies (GWAS)	Comparing the frequency of combinations of alleles at nearby loci in a given population to identify genetic variants associated with complex diseases

Box 8.14 Influences on decisions regarding options for genetic counselling

- Magnitude of risk
- Perceived severity of disorder
- Availability of treatment
- Person's experience of the disorder
- Family size
- Availability of a safe and reliable prenatal diagnostic test
- Parental cultural, religious or ethical values.

Chapter 9: Perinatal medicine

Summary
Maternal diabetes

- Meticulous control pre-conceptually and during pregnancy markedly reduces fetal and neonatal morbidity and mortality.
- The fetus may be macrosomic because of fetal hyperglycaemia resulting in hyperinsulinism, or growth-restricted secondary to maternal microvascular disease, and is at increased risk of congenital malformations.
- The macrosomic infant is at increased risk of asphyxia and birth trauma from obstructed labour or delivery.
- The newborn infant is prone to hypoglycaemia and polycythaemia.

Table 9-1. Maternal medication which may adversely affect the fetus

Medication	Adverse effect on fetus
Anticonvulsant therapy with carbamazepine, valproic acid (sodium valproate) or hydantoins (phenytoin)	Fetal carbamazepine/valproate/hydantoin syndrome - midfacial hypoplasia, CNS, limb and cardiac malformations, developmental delay
Cytotoxic agents	Congenital malformations
Diethylstilboestrol (DES)	Clear-cell adenocarcinoma of vagina and cervix
Iodides/propylthiouracil	Goitre, hypothyroidism
Lithium	Congenital heart disease
Tetracycline	Enamel hypoplasia of the teeth
Thalidomide	Limb shortening (phocomelia)
Vitamin A and retinoids	Increased spontaneous abortions, abnormal face
Warfarin	Interferes with cartilage formation (nasal hypoplasia and epiphyseal stippling); cerebral haemorrhages and microcephaly

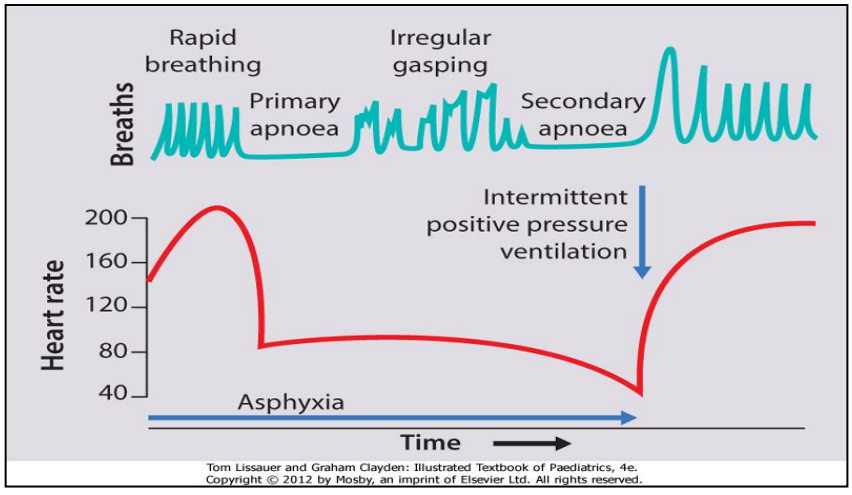


Figure 9.8 Changes in respiration and heart rate with continuous asphyxia. Once the infant has stopped gasping in secondary apnoea, resuscitation with lung expansion is required to establish regular respiration and restore the circulation.

Table 9-2. The Apgar score

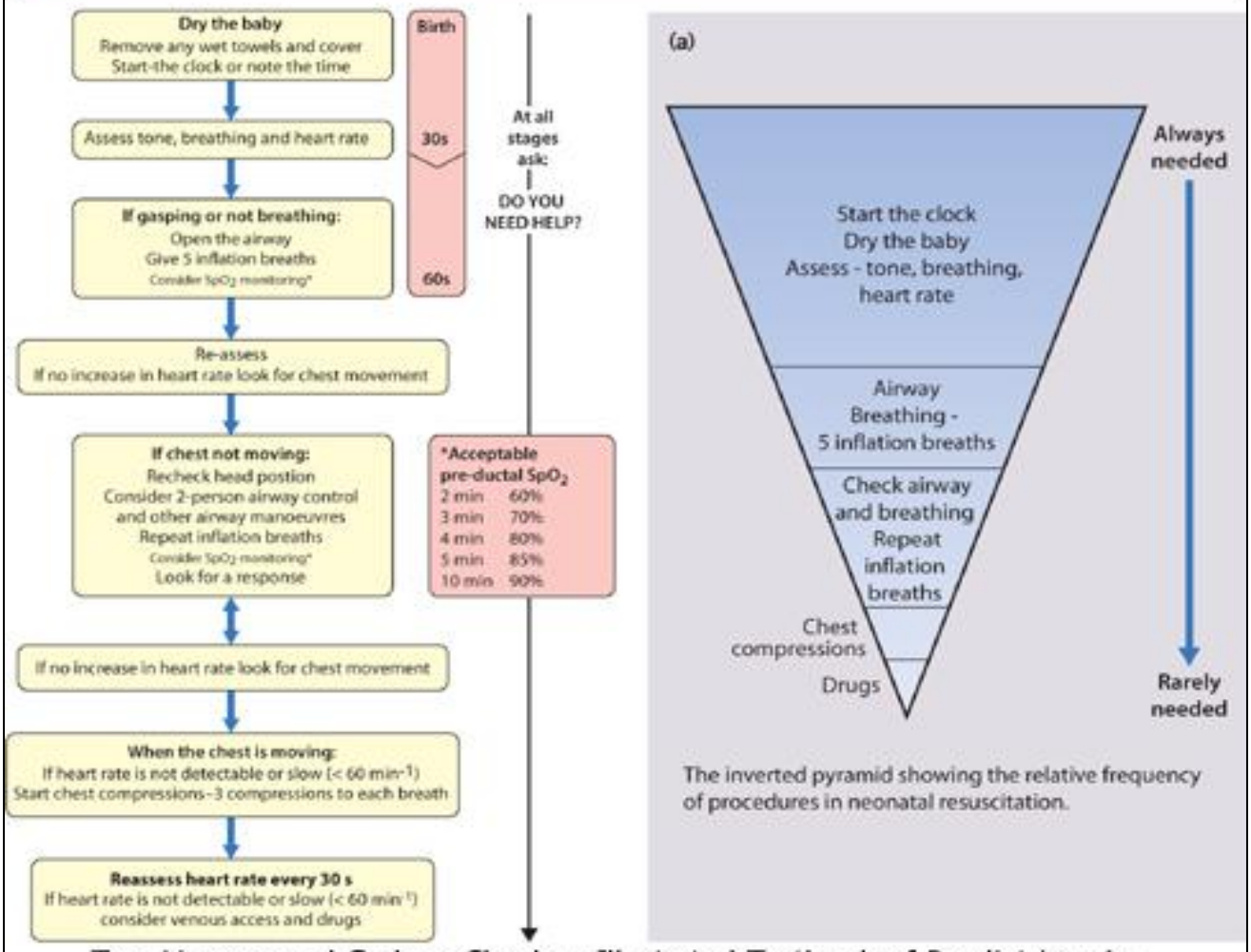
	Score 0	1	2
Heart rate	Absent	<100 beats/min	≥100 beats/min
Respiratory effort	Absent	Gasping or irregular	Regular, strong cry
Muscle tone	Flaccid	Some flexion of limbs	Well flexed, active
Reflex irritability	None	Grimace	Cry, cough
Colour	Pale/blue	Body pink, extremities blue	Pink

Neonatal resuscitation – Preparation and overview

Preparation

- All health professionals dealing with newborn infants should be proficient in basic resuscitation; i.e. **A**irway, **B**reathing with mask ventilation, **C**irculation with cardiac compressions
- Additional skilled assistance is needed if the baby does not respond rapidly and should be called without delay
- A person proficient in advanced resuscitation (**A**irway, **B**reathing via tracheal ventilation, **C**irculation, **D**rugs) should be on site and available at short notice in a maternity unit at all times
- The need for resuscitation can usually be anticipated and a person proficient in advanced resuscitation should be in attendance at all high-risk deliveries
- A clock should be started at birth for accurate timing of changes in the infant's condition
- Keep the infant warm. Dry, remove wet towel and replace with dry one. This will also provide stimulation. Can place directly on mother's chest and covered if crying, good tone and colour and desired by the mother
- Resuscitation should be performed under a radiant warmer
- If preterm and <30 weeks' gestation, to avoid heat loss, place the infant in a plastic bag without drying but under a radiant warmer and on a warming mattress. Leave the head exposed and cover with a woollen hat.
- Assess the infant's condition. Is the baby breathing or crying, good heart rate (120–160 beats/min, best assessed by listening with a stethoscope), good colour and muscle tone?
- If not, commence neonatal resuscitation

Overview



The inverted pyramid showing the relative frequency of procedures in neonatal resuscitation.

Neonatal resuscitation - Airway and breathing

Airway and Breathing

Airway

- Opened by placing the infants's head in a neutral position **(b)**
- Provide chin lift or jaw thrust if necessary **(c)**
- Suction any blood or secretions
- Consider placing a Guedel airway

Breathing – mask ventilation

- If not breathing adequately, start mask ventilation
- Mask is placed over mouth and nose **(d)** and connected to flow-controlled pressure-limited circuit (e.g. mechanical ventilator or Neopuff) or self-inflating bag **(e)**
- Head in neutral position
- Give 5 inflation breaths, inflation time 2–3 seconds at inspiratory pressure of 30 cm H_2O in term infants to expand lungs
- If heart rate increases, but breathing does not start, continue with peak inspiratory pressure to achieve chest wall movement (15–25 cm H_2O, 0.5 second inflation time) and rate of 30–40 breaths/min
- Begin ventilatory resuscitation in air to avoid excessive tissue oxygenation. If giving additional oxygen, use air/oxygen blender to titrate oxygen concentration with oxygen saturation on pulse oximeter. (Acceptable pre-ductal saturations – 2 min 60%; 3 min 70%; 4 min 80%; 5 min 85%; 10 min 90%.)
- Reassess every 30 seconds. If heart rate not responding, check mask position, neck position, is jaw thrust needed, is circuit all right, ensure adequate chest movement. Consider using two-person airway control **(f)**. Call for help

Intubation

- Intubation and mechanical ventilation **(g)** are indicated if: mask ventilation is ineffective, tracheal suction needed to clear an obstructed airway, congenital upper airway abnormality, extreme prematurity-for giving surfactant.
- Limit intubation attempts to 20–30 seconds.

(b) Head position, vital for airway management

i) Head in correct airway position ii) Head over-extended – incorrect
iii) Head flexed – incorrect

(c)

Chin support Jaw thrust

(d) Correct size and position of the face mask. It should cover the mouth, nose and chin

Correct
Covers mouth, nose and chin but not eyes

Incorrect
Too large – covers eyes and extends over chin

Incorrect
Too small – does not cover nose and mouth completely

(e) Mask ventilation

Mask ventilation delivered with pressure-limited circuit via T-piece (as shown), Neopuff or self-inflating bag.

(f) Two-person airway control

Consider if mask inflation ineffective. One person holds the head in the correct position, applies jaw thrust and holds the mask in place. The assistant operates the T-piece to provide lung inflation.

(g) Tracheal intubation

The laryngoscope blade is lifted upwards. Gentle pressure on the trachea helps bring the vocal cords into view

Neonatal resuscitation – Circulation and Drugs

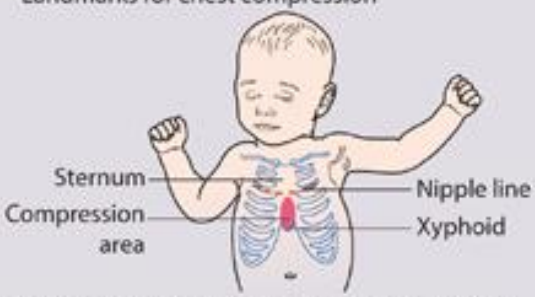
Circulation

Chest compression (h, i and j)

- Start if heart rate < 60 beats/min in spite of effective lung inflation
- Ratio of compression: lung inflation of 3:1, rate of 90 compressions: 30 breaths/min (120 events/min)
- Recheck heart rate every 30 seconds; stop when heart rate >60 beats/min

(h) Chest compression

Landmarks for chest compression



Apply pressure to lower third of sternum, just below imaginary line joining the nipples. Depress to reduce antero-posterior diameter by one-third (1–1.5 cm).

(i)

Thumb technique, with hands encircling the chest. In larger infants thumbs can be placed side by side.

(j)

Two finger technique – less effective but easier if alone.

Volume and drugs

Consider drugs **(k)** if heart rate <60 beats/min in spite of adequate ventilation and chest compression, though evidence for their efficacy is lacking

Rarely needed.

Drugs should be given via an umbilical venous catheter, or, if not possible, via an intra-osseous needle.

Drugs given via a peripheral vein are unlikely to reach the heart. Giving standard doses of epinephrine (adrenaline) down the endotracheal tube does not appear to be effective, so drug dosage is increased for this route.

A newborn baby who looks white and has poor skin and peripheral perfusion due to acidosis and peripheral vasoconstriction may have had acute blood loss. There may be a history of antepartum haemorrhage or acute twin-to-twin transfusion. Immediate blood transfusion with Group O rhesus negative blood is required.

(k) Drugs used in neonatal resuscitation

Drug	Concentration	Route/dosage	Indications
Epinephrine (adrenaline)	1:10 000	IV: 0.1 ml/kg (10 micrograms/kg), then 0.1– 0.3 ml/kg (10–30 micrograms/kg) ET: 1ml/kg (100 micrograms/kg) i.e. 10 times the IV dose, whilst IV access is obtained	Heart rate <60 beats/min in spite of adequate ventilation and external cardiac compression
Sodium bicarbonate	4.2%	2–4 ml/kg (1–2 mmol/kg)	Severe lactic acidosis
Dextrose	10%	2.5 ml/kg (250 mg/kg)	Hypoglycaemia
Volume expander	Normal saline Blood	10 ml/kg, repeat if necessary	Blood loss

Summary
Size at birth

- Small for gestational age - birthweight <10th centile
- Intrauterine growth restriction (IUGR) - fails to reach genetically determined growth potential
- Growth restriction - symmetrical or asymmetrical, but often mixed.

Routine examination of the newborn infant

Box 9.4 Routine examination of the newborn.
Birthweight, gestational age and birthweight centile are noted.

General observation of the baby's appearance, posture and movements provides valuable information about many abnormalities. The baby must be fully undressed during the examination.

The head circumference is measured with a paper tape measure and its centile noted. This is a surrogate measure of brain size.

The fontanelle and sutures are palpated. The fontanelle size is very variable. The sagittal suture is often separated and the coronal sutures may be overriding. A tense fontanelle when the baby is not crying may be due to raised intracranial pressure and cranial ultrasound should be performed to check for hydrocephalus. A tense fontanelle is also a late sign of meningitis.

The face is observed. If abnormal, this may represent a syndrome, particularly if other anomalies are present. Down syndrome is the most common, but there are hundreds of syndromes. When the diagnosis is uncertain, a book or a computer database may be consulted and advice should be sought from a senior paediatrician or geneticist.

If plethoric or pale, the haematocrit should be checked to identify polycythaemia or anaemia. Central cyanosis, which always needs urgent assessment, is best seen on the tongue.

Jaundice within 24 h of birth requires further evaluation.

The eyes are checked for red reflex with an ophthalmoscope. If absent, may be from cataracts, retinoblastoma and corneal opacity. This reflex is not present in infants with pigmented skin, but the retinal vessels can be visualised.

The palate needs to be inspected, including posteriorly to exclude a posterior cleft palate, and palpated to detect an indentation of the posterior palate from a submucous cleft.

Breathing and chest wall movement are observed for signs of respiratory distress.

On auscultating the heart, the normal rate is 110-160 beats/min in term babies, but may drop to 85 beats/min during sleep.

On palpating the abdomen, the liver normally extends 1-2 cm below the costal margin, the spleen tip may be palpable, as may the kidney on the left side. Any intra-abdominal masses, which are usually renal in origin, need further investigation.

The femoral pulses are palpated. Their pulse pressure is:

- - reduced in coarctation of the aorta. This can be confirmed by measuring the blood pressure in the arms and legs
- - increased if there is a patent ductus arteriosus.

The genitalia and anus are inspected on removing the nappy. Patency of the anus is confirmed. In boys, the presence of testes in the scrotum is checked by palpation.

Muscle tone is assessed by observing limb movements. Most babies will support their head briefly when the trunk is held vertically.

The whole of the back and spine is observed, looking for any midline defects of the skin.

The hips are checked for developmental dysplasia of the hips (DDH). This is left until last as the procedure is uncomfortable.

Lesions in newborn infants that resolve spontaneously

Box 9.5 Lesions in newborn infants that resolve spontaneously
Peripheral cyanosis of the hands and feet - common in the first day

Traumatic cyanosis from a cord round the baby's neck or from a face or brow presentation - causes blue discoloration of the skin, petechiae over the head and neck or affected part but not the tongue

Swollen eyelids and distortion of shape of the head from the delivery

Subconjunctival haemorrhages - occur during delivery

Small white pearls along the midline of the palate (Epstein pearls)

Cysts of the gums (epulis) or floor of the mouth (ranula)

Breast enlargement - may occur in newborn babies of either sex (Fig. 9.13a). A small amount of milk may be discharged

White vaginal discharge or small withdrawal bleed in girls. There may be a prolapse of a ring of vaginal mucosa

Capillary haemangioma or 'stork bites' - pink macules on the upper eyelids, mid-forehead and nape of the neck are common and arise from distension of the dermal capillaries. Those on the eyelids gradually fade over the first year; those on the neck become covered with hair

Neonatal urticaria (erythema toxicum) - a common rash appearing at 2-3 days of age, consisting of white pinpoint papules at the centre of an erythematous base (Fig. 9.13b). The fluid contains eosinophils. The lesions are concentrated on the trunk; they come and go at different sites

Milia - white pimples on the nose and cheeks, from retention of keratin and sebaceous material in the pilaceous follicles (Fig. 9.13c)

Mongolian blue spots - blue/black macular discoloration at the base of the spine and on the buttocks (Fig. 9.13d); occasionally occur on the legs and other parts of the body. Usually but not invariably in Afro-Caribbean or Asian infants. They fade slowly over the first few years. They are of no significance unless misdiagnosed as bruises

Umbilical hernia - common, particularly in Afro-Caribbean infants. No treatment is indicated as it usually resolves within the first 2-3 years

Positional talipes - the feet often remain in their in-utero position. Unlike true talipes equinovarus, the foot can be fully dorsiflexed to touch the front of the lower leg (Fig. 9.13e,f)

Caput succedaneum (see Fig. 10.6).

Some significant abnormalities detected on routine examination

Box 9.6 Some significant abnormalities detected on routine examination
Port-wine stain (naevus flammeus). Present from birth and usually grows with the infant (Fig. 9.14a). It is due to a vascular malformation of the capillaries in the dermis. Rarely, if along the distribution of the trigeminal nerve, it may be associated with intracranial vascular anomalies (Sturge-Weber syndrome), or severe lesions on the limbs with bone hypertrophy (Klippel-Trenaunay syndrome). Disfiguring lesions can now be improved with laser therapy.

Strawberry naevus (cavernous haemangioma). Often not present at birth, but appear in the first month of life and may be multiple (Fig. 9.14b). It is more common in preterm infants. It increases in size until 3-15 months old, then gradually regresses. No treatment is indicated unless the lesion interferes with vision or the airway. Ulceration or haemorrhage may occur. Thrombocytopenia may occur with large lesions, when therapy with systemic steroids or interferon-α may be required.

Natal teeth consisting of the front lower incisors - may be present at birth. If loose, they should be removed to avoid the risk of aspiration.

Extra digits - are sometimes connected by a thin skin tag but may be completely attached containing bone (Fig. 9.14c) and should ideally be removed by a plastic surgeon or else tied off at its base. Skin tags anterior to the ear and accessory auricles should be removed by a plastic surgeon.

Heart murmur - poses a difficult problem, as most murmurs audible in the first few days of life resolve shortly afterwards. However, some are caused by congenital heart disease. If there are any features of a significant murmur (see Ch. 17), upper and lower limb blood pressures, and pre- and post-ductal pulse oximetry should be checked followed by an echocardiogram. Otherwise, a follow-up examination is arranged and the parents warned to seek medical assistance if their baby feeds poorly, develops laboured breathing or becomes cyanosed.

Midline abnormality over the spine or skull, such as a tuft of hair, swelling or naevus - requires further evaluation as it may indicate an underlying abnormality of the vertebrae, spinal cord or brain.

Palpable and large bladder - if there is urinary outflow obstruction, particularly in boys with posterior urethral valves. Requires prompt evaluation with ultrasound.

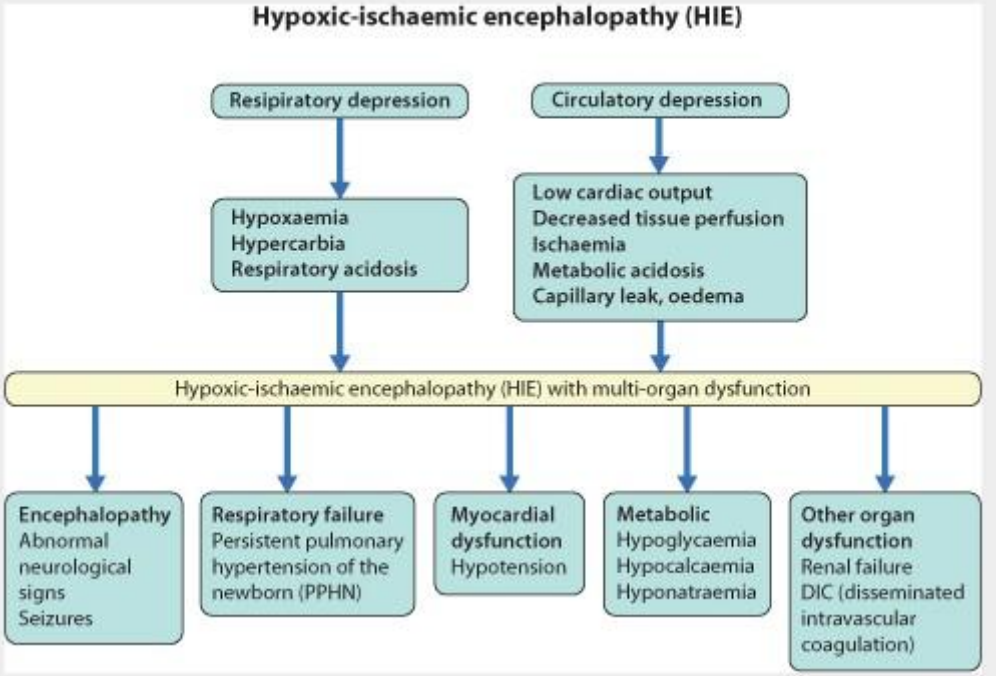
Talipes equinovarus - which cannot be corrected as in positional talipes.

After tracheal intubation, if the heart rate does not increase and adequate chest movement is not achieved, consider 'DOPE':

- **D**isplaced tube: often in the oesophagus or right main bronchus
- **O**bstructed tube: especially meconium
- **P**atient:
    - tracheal obstruction
    - - lung disorders: lung immaturity or respiratory distress syndrome, pneumothorax, diaphragmatic hernia, lung hypoplasia, pleural effusion
    - - shock from blood loss
    - - birth asphyxia or trauma
    - - upper airways obstruction: choanal atresia.
- **E**quipment failure: gas supply exhausted or disconnected.

Chapter 10: Neonatal medicine

Summary



Box 10.1 Medical problems of preterm infants

- Need for resuscitation at birth
- Respiratory
  - - Respiratory distress syndrome (RDS)
  - - Pneumothorax
  - - Apnoea and bradycardia
- Hypotension
- Patent ductus arteriosus
- Temperature control
- Metabolic
  - - Hypoglycaemia
  - - Hypocalcaemia
  - - Electrolyte imbalance
  - - Osteopenia of prematurity
- Nutrition
- Infection
- Jaundice
- Intraventricular haemorrhage/periventricular leukomalacia
- Necrotising enterocolitis
- Retinopathy of prematurity
- Anaemia of prematurity
- Iatrogenic
- Bronchopulmonary dysplasia (chronic lung disease)
- Inguinal hernias.

Stabilising preterm or sick infants

Airway, breathing

- Respiratory distress: tachypnoea, laboured breathing with chest wall recession, nasal flaring, expiratory grunting, cyanosis
- Apnoea

Management, as required:

- Clear the airway
- Oxygen
- High-flow humidified oxygen therapy
- CPAP (continuous positive airway pressure)
- Mechanical ventilation

Monitoring

- Oxygen saturation (maintain at 88-95% if preterm)
- Heart rate
- Respiratory rate
- Temperature
- Blood pressure
- Blood glucose
- Blood gases
- Weight

Temperature control

- Place in plastic bag at birth to keep warm if extremely preterm
- Perform stabilisation under a radiant warmer or in a humidified incubator to avoid hypothermia.

Venous and arterial lines

Peripheral intravenous line

Required for intravenous fluids, antibiotics and other drugs.

Umbilical venous catheter

May be used for intravenous access at resuscitation, in extremely preterm infants for the first few days or to administer high osmolality fluids (e.g. high-concentration dextrose) or medications needing central delivery (e.g. inotropes).

Arterial line

- Inserted if frequent blood gas analysis, blood tests and continuous blood pressure monitoring are required. Usually umbilical artery catheter (UAC), sometimes peripheral cannula if for short period or no umbilical artery catheter possible.
- The arterial oxygen tension is maintained at 8-12 kPa (60-90 mmHg) and the CO_2 tension at 4.5-6.5 kPa (35-50 mmHg). Continuous non-invasive transcutaneous arterial blood gas monitoring may also be used.

Central venous line for parenteral nutrition, if indicated

Inserted peripherally when infant is stable.

Chest X-ray with or without abdominal X-ray

Assists in the diagnosis of respiratory disorders and to confirm the position of the tracheal tube and central lines.

Investigations

- Haemoglobin, neutrophil count, platelet count
- Blood urea, creatinine, electrolytes and lactate
- Culture - blood ± CSF ± urine
- Blood glucose
- CRP/acute phase reactant
- Coagulation screen if indicated

Antibiotics

Broad-spectrum antibiotics are given.

Minimal handling

All procedures, especially painful ones, adversely affect oxygenation and the circulation. Handling the infant is kept to a minimum and done as gently, rapidly and efficiently as possible. Analgesia should be provided to prevent pain as necessary.

Parents

Although medical and nursing staff are usually fully occupied stabilising the baby, time must be found for parents and immediate relatives to allow them to see and touch their baby and to be kept fully informed.

Table 10-1. The preterm infant compared with the term infant

Gestation	23-27 weeks	Term (37-42 weeks)
Birthweight (50th centile)	At 24 weeks - male 700 g, female 620 g	At 40 weeks - male 3.55 kg, female 3.4 kg
Skin	Very thin (Fig. 10.9a)	Thick skin (Fig. 10.9b)
	Dark red colour all over body	Pale pink colour
Ears	Pinna soft, no recoil	Pinna firm, cartilage to edge, immediate recoil
Breast tissue	No breast tissue palpable	One or both nodules >1 cm
Genitalia	Male - scrotum smooth, no testes in scrotum	Male - scrotum has rugae, testes in scrotum
	Female - prominent clitoris, labia majora widely separated, labia minora protruding	Female - labia minora and clitoris covered
Breathing	Needs respiratory support. Apnoea common	Rarely needs respiratory support. Apnoea rare
Sucking and swallowing	No coordinated sucking	Coordinated (from 34-35 weeks)
Feeding	Usually needs TPN (total parenteral nutrition), then tube feeding	Cries when hungry. Feeds on demand
Cry	Faint	Loud
Vision, interaction	Eyelids may be fused. Infrequent eye movements. Not available for interaction	Makes eye contact, alert wakefulness
Hearing	Startles to loud noise	Responds to sound
Posture	Limbs extended, jerky movements	Flexed posture, smooth movements

Respiratory distress syndrome

- Common in very preterm infants
- Caused by surfactant deficiency
- Antenatal corticosteroids and surfactant therapy markedly reduce morbidity and mortality.

Temperature control
Prevention of heat loss in newborn infants

1. Convection

- Raise temperature of ambient air in incubator
- Clothe, including covering head
- Avoid draughts

2. Radiation

- Cover baby
- Double walls for incubators

3. Evaporation

- Dry and wrap at birth; if extremely preterm place baby's body directly into plastic bag at birth
- Humidify incubator

4. Conduction

- Nurse on heated mattress.

Birth injuries

Soft tissue injuries
- Caput succedaneum, cephalhaematoma, chignon, bruises and abrasions
- Subaponeurotic haemorrhage

Nerve palsies
- Brachial plexus - Erb palsy
- Facial nerve palsy

Fractures
- Clavicle, humerus, femur

Summary of problems of very low birthweight infants (<1.5 kg)

Respiratory

Respiratory distress syndrome (surfactant deficiency)(74%)
- respiratory distress within 4 hours of birth
- antenatal corticosteroids and surfactant therapy reduce morbidity and mortality
- oxygen therapy, but excess may damage the retina
- nasal CPAP (continuous positive airway pressure) (67%) and mechanical ventilation (64%) - often required to expand lungs and prevent lung collapse

Pneumothorax (4%)
Apnoea and bradycardia and desaturations
Bronchopulmonary dysplasia (chronic lung disease) – O_2 requirement at 36 weeks post-menstrual age (27%)

Circulation

Hypotension – may require volume support, intropes or corticosteroids
Patent ductus arteriosus – needing medical treatment (34%) or surgical ligation (8%)

Nutrition

Nasogastric tube feeding – until 35–36 weeks post-menstrual age
Feeding intolerance - TPN (total parenteral nutrition) often required

Gastrointestinal

Necrotising enterocolitis (6%)
– serious, management is medical or surgery for bowel necrosis or perforation

Metabolic

Hypoglycaemia – common
Electrolyte disturbances
Osteopenia of prematurity from phosphate deficiency

Hearing

Checked before discharge

Jaundice – common, low treatment threshold

Anaemia

Often need blood transfusions

Eyes

Retinopathy of prematurity – may need laser therapy (4%)

Temperature control

Avoid hypothermia
Nurse in neutral thermal environment
Nurse in incubator or under radiant warmer
Clothe if possible
Humidity reduces evaporative heat loss

Infection

Common and potentially serious (25%)
Increased risk of early-onset infection – group B streptococcus
Main problem is nosocomial infection – mainly coagulase-negative staphylococcus, also fungal and other infections

Brain injury

Haemorrhage (25%)
- germinal layer, intraventricular, parenchymal

Ventricular dilatation – may need ventriculo-peritoneal shunt
Periventricular leukomalacia (3%)
– ischaemic white matter injury

Following discharge

Specialist community nursing support helpful, if available
Increased risk of respiratory infection and wheezing – especially from bronchiolitis (caused by respiratory syncitial virus, RSV) and pertussis; may need intensive care
Consider prophylaxis against RSV infection
Increased rehospitalisation – respiratory disorders, inguinal hernias
Monitor growth, development (for learning disorders, co-ordination, cerebral palsy), behaviour, attention, vision, hearing – increased risk of impairment

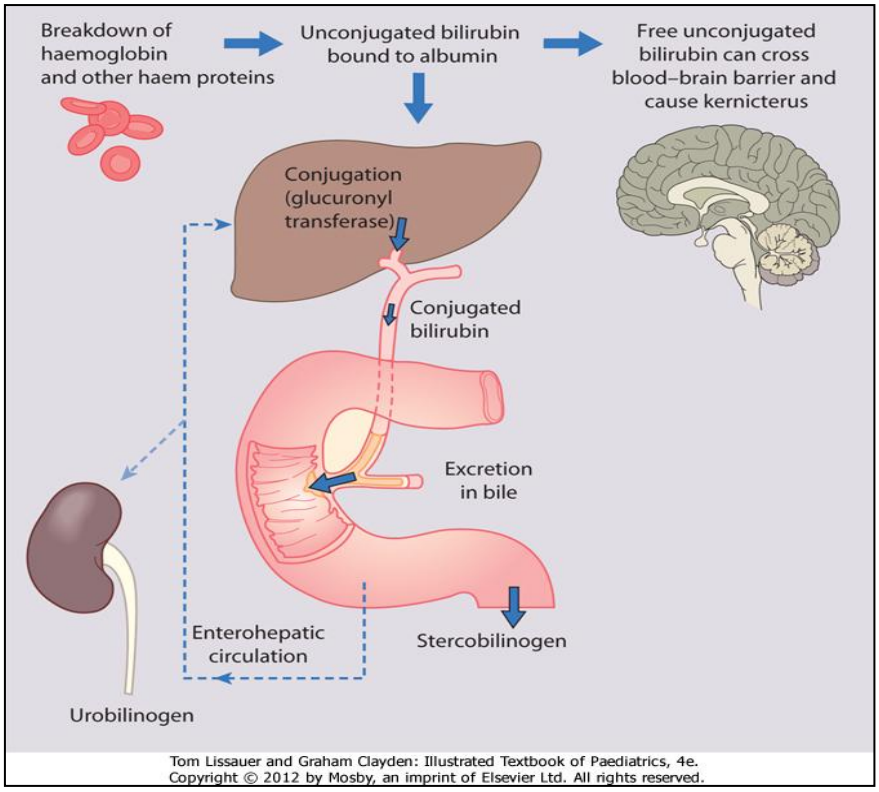


Figure 10.19 The breakdown product of haemoglobin is unconjugated bilirubin (indirect bilirubin), which is insoluble in water but soluble in lipids. It is carried in the blood bound to albumin. When the albumin binding is saturated, free unconjugated bilirubin can cross the blood-brain barrier, as it is lipid soluble. Unconjugated bilirubin bound to albumin is taken up by the liver and conjugated by the enzyme glucuronyl transferase to conjugated bilirubin (direct bilirubin), which is water-soluble and excreted in bile into the gut and is detectable in urine when blood levels rise. Reabsorption of bilirubin from the gut (enterohepatic circulation) is increased when milk intake is low.

Table 10-2. Causes of neonatal jaundice

Jaundice starting at <24 h of age	*Haemolytic disorders:*
	Rhesus incompatibility
	ABO incompatibility
	G6PD deficiency
	Spherocytosis, pyruvate kinase deficiency
	Congenital infection
Jaundice at 24 h to 2 weeks of age	Physiological jaundice
	Breast milk jaundice
	Infection, e.g. urinary tract infection
	Haemolysis, e.g. G6PD deficiency, ABO incompatibility
	Bruising
	Polycythaemia
	Crigler-Najjar syndrome
Jaundice at >2 weeks of age	*Unconjugated:*
	Physiological or breast milk jaundice
	Infection (particularly urinary tract)
	Hypothyroidism
	Haemolytic anaemia, e.g. G6PD deficiency
	High gastrointestinal obstruction, e.g. pyloric stenosis
	Conjugated (>25 μmol/L):
	Bile duct obstruction
	Neonatal hepatitis

Assessment of neonatal jaundice

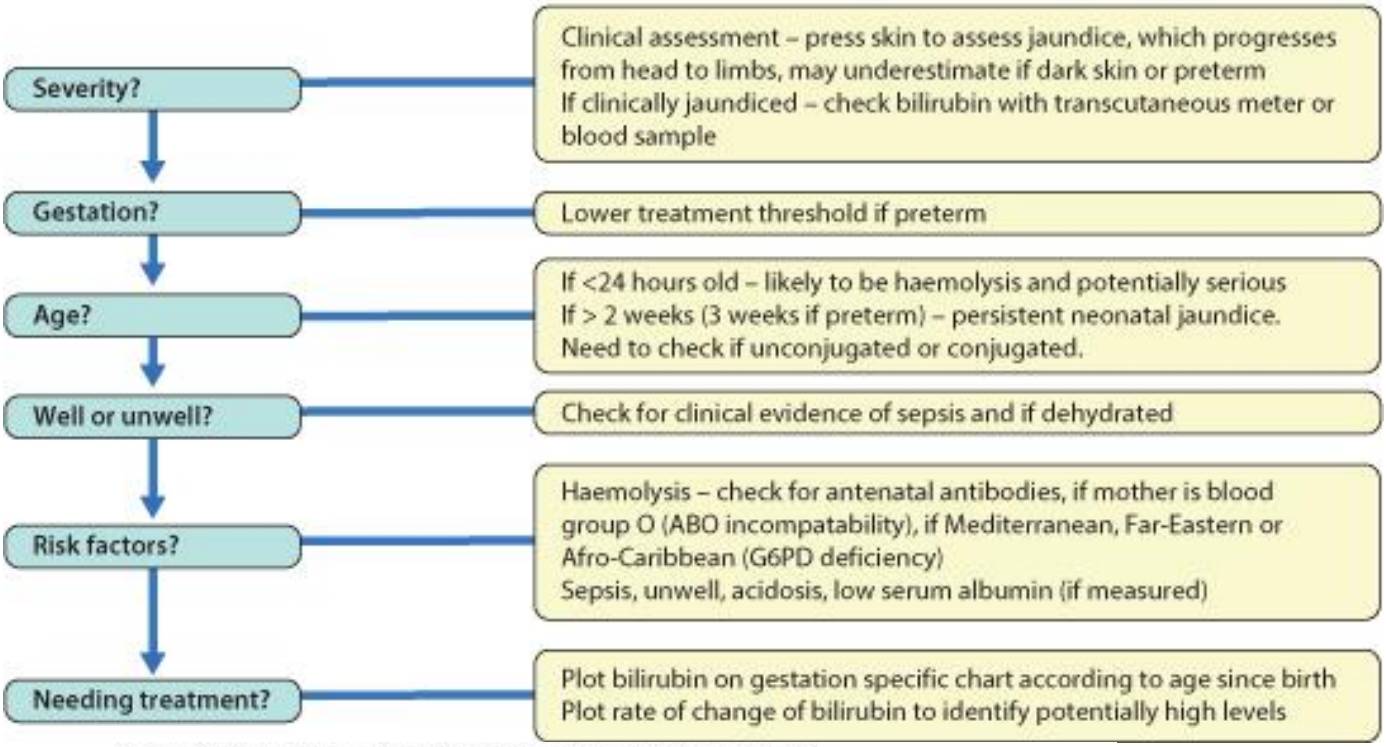


Table 10-3. Causes of respiratory distress in term infants

Pulmonary	
Common	Transient tachypnoea of the newborn
Less common	Meconium aspiration
	Pneumonia
	Respiratory distress syndrome
	Pneumothorax
	Persistent pulmonary hypertension of the newborn
	Milk aspiration
Rare	Diaphragmatic hernia
	Tracheo-oesophageal fistula (TOF)
	Pulmonary hypoplasia
	Airways obstruction, e.g. choanal atresia
	Pulmonary haemorrhage
Non-pulmonary	
	Congenital heart disease
	Intracranial birth trauma/encephalopathy
	Severe anaemia
	Metabolic acidosis

Box 10.2 Clinical features of neonatal sepsis

- Fever or temperature instability or hypothermia
- Poor feeding
- Vomiting
- Apnoea and bradycardia
- Respiratory distress
- Abdominal distension
- Jaundice
- Neutropenia
- Hypo-/hyperglycaemia
- Shock
- Irritability
- Seizures
- Lethargy, drowsiness
- *In meningitis:*
- Tense or bulging fontanelle
- Head retraction (opisthotonos)

Box 10.3 Causes of neonatal seizures

- Hypoxic-ischaemic encephalopathy
- Cerebral infarction
- Septicaemia/meningitis
- Metabolic
  - - Hypoglycaemia
  - - Hypo-/hypernatraemia
  - - Hypocalcaemia
  - - Hypomagnesaemia
  - - Inborn errors of metabolism
  - - Pyridoxine dependency
- Intracranial haemorrhage
- Cerebral malformations
- Drug withdrawal, e.g. maternal opiates
- Congenital infection
- Kernicterus

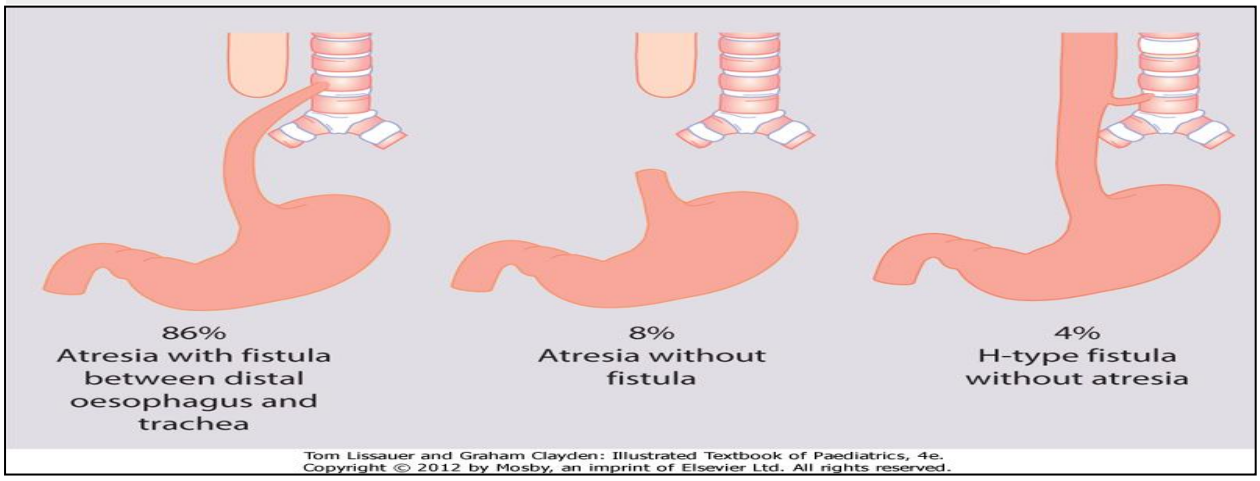


Figure 10.26 Oesophageal atresia and tracheo-oesophageal fistula.

Chapter 11: Growth and puberty

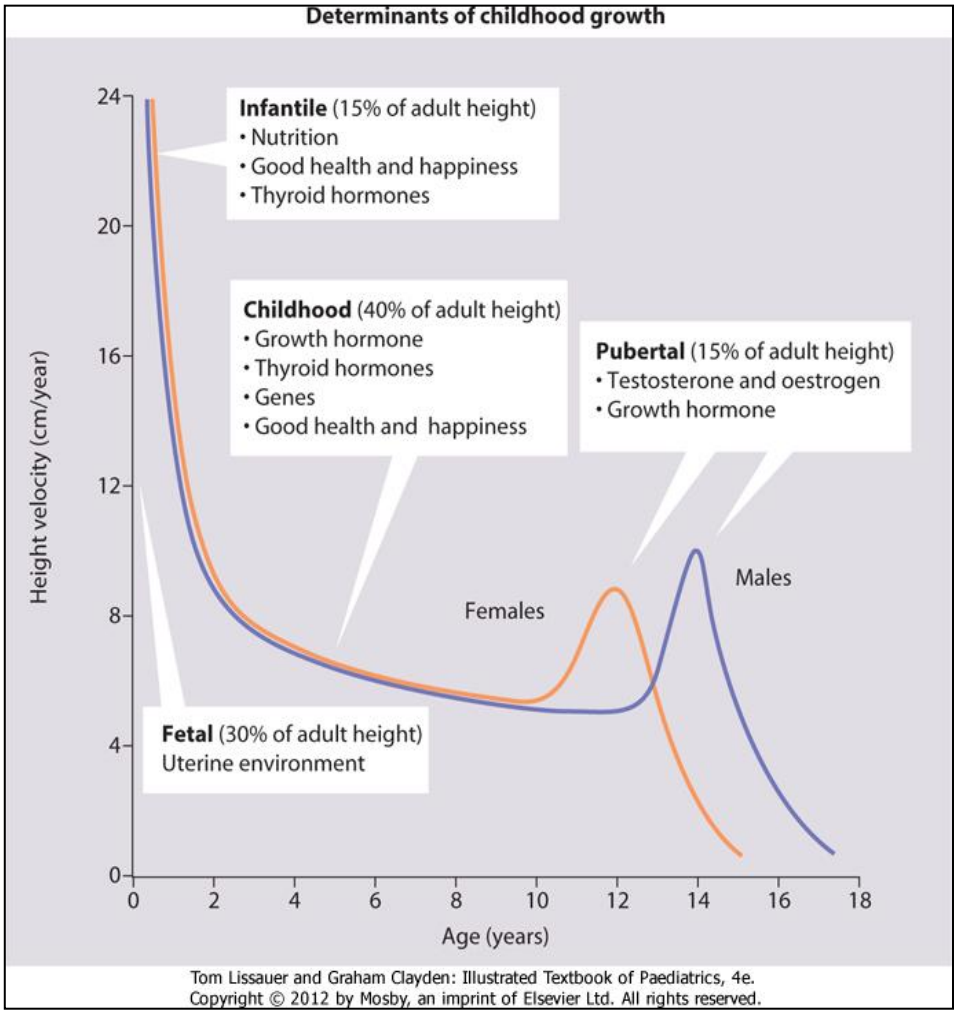


Figure 11.1 Male and female height velocity charts (50th percentile) showing the determinants of childhood growth. The fetal and infantile phases are mainly dependent on adequate nutrition, whereas the childhood and pubertal phases are dependent on growth hormone and other hormones. Adult males are taller than females as they have a longer childhood growth phase, their peak height velocity is higher and their growth ceases later.

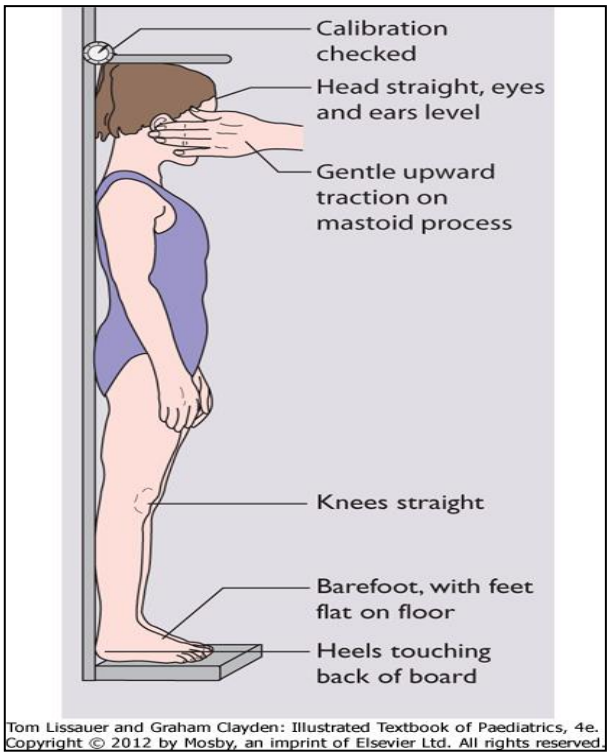
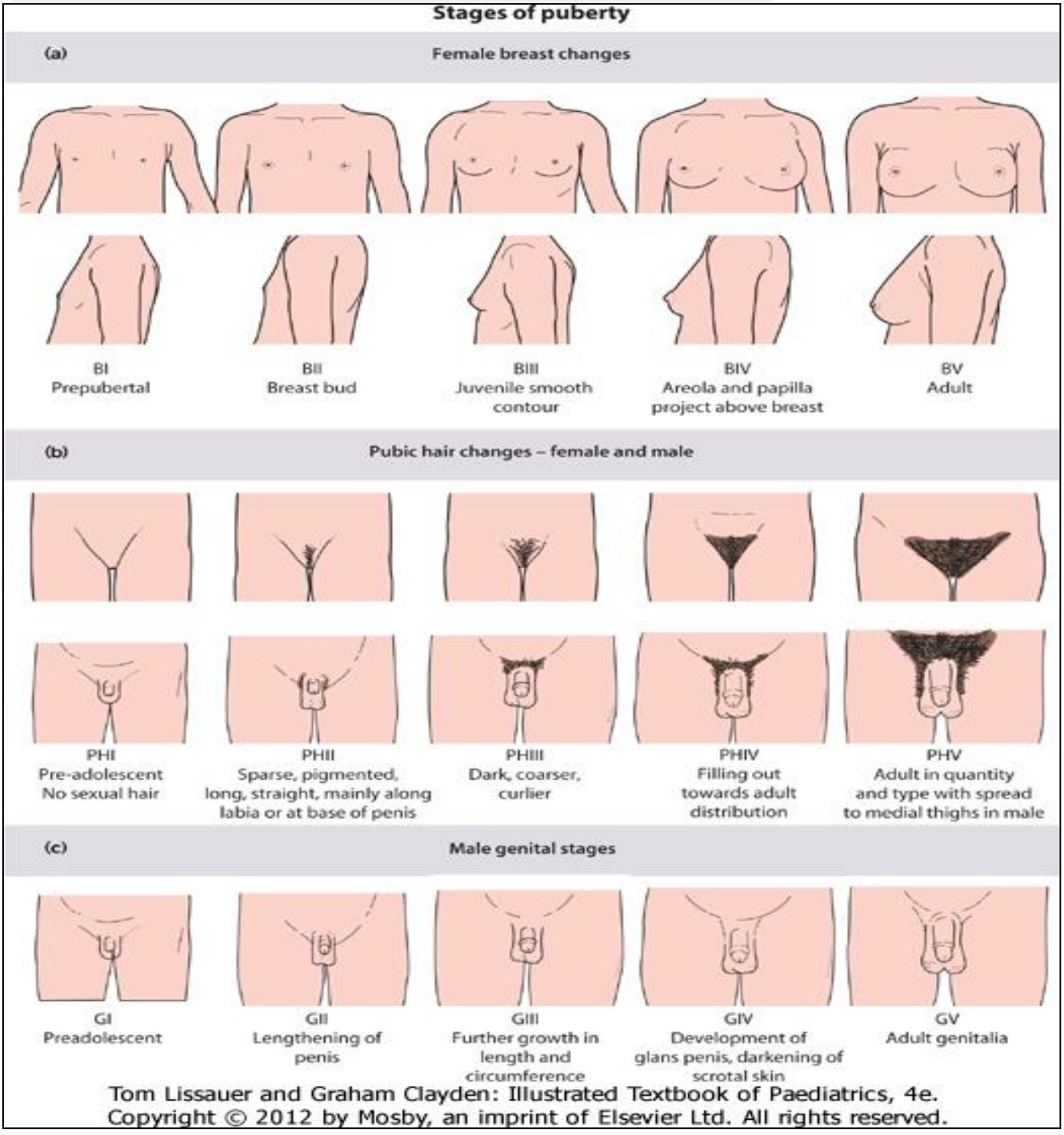
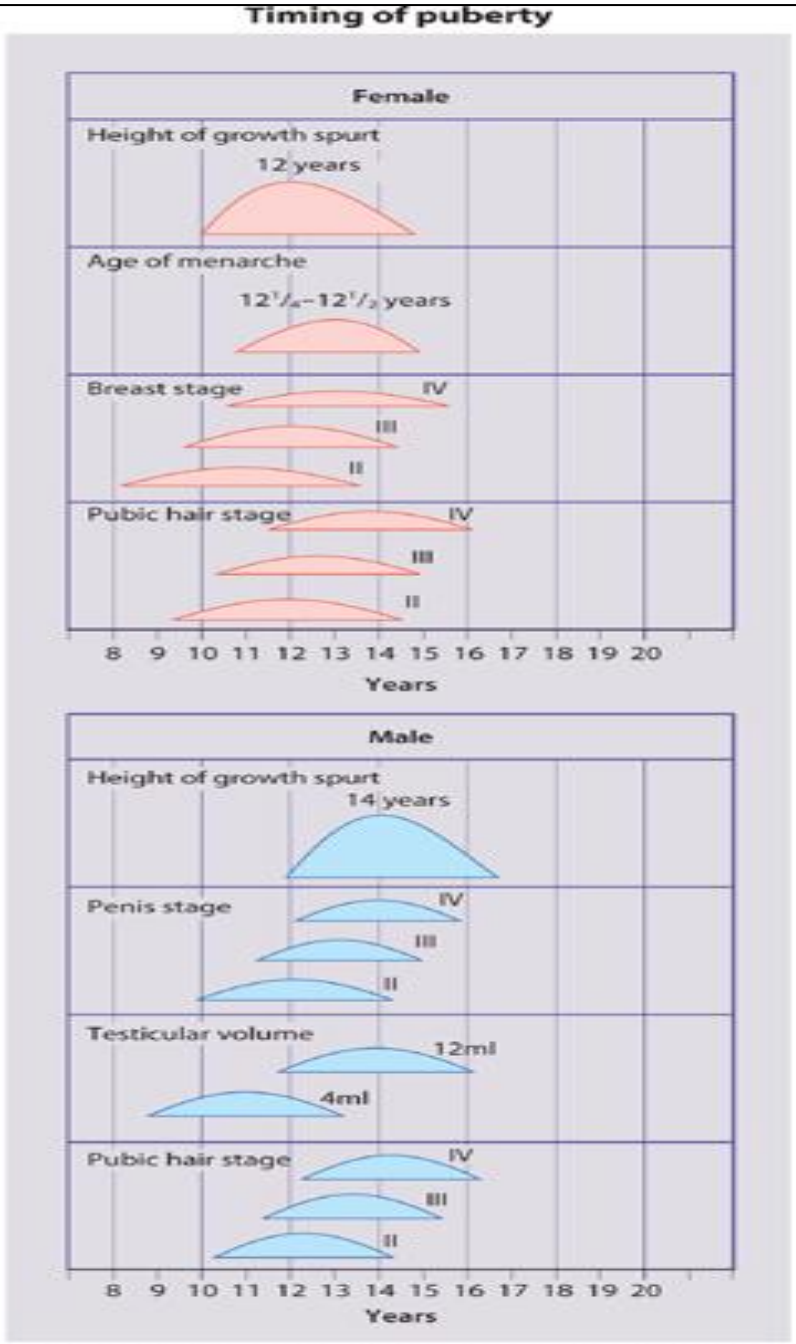


Figure 11.2 Measuring height accurately in children.

Summary
Measurement of children

- Measurement must be accurate for meaningful monitoring of growth
- Growth parameters should be plotted on charts
- Significant abnormalities of height are:
  - - measurements outside the 0.4th or 99.6th centiles if the mid-parental height is not short or tall
  - - if markedly discrepant from weight
  - - serial measurements which cross growth centile lines after the first year of life.





Summary
Puberty

- The first sign in females is breast development; in males it is testicular enlargement.
- In females the height spurt occurs shortly after breast development; in males it starts almost 18 months after the first signs of puberty.

Causes & evaluation of short stature

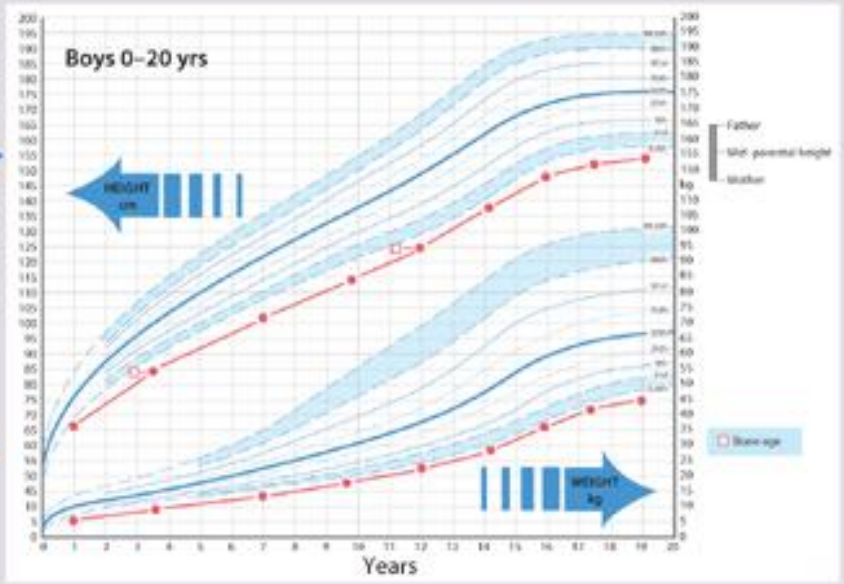
(a) Familial → Following growth centile within predicted range for parental height

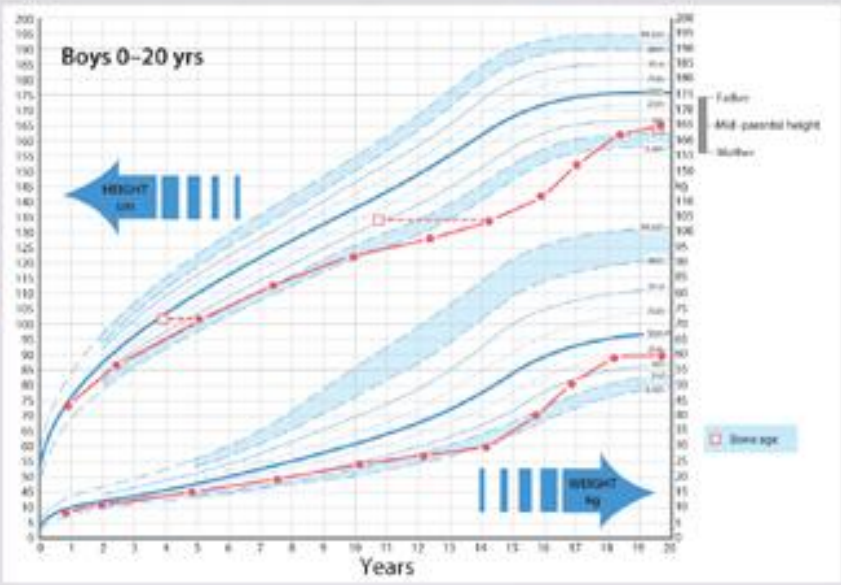
(b) Severe intrauterine growth restriction or prematurity → Short from birth

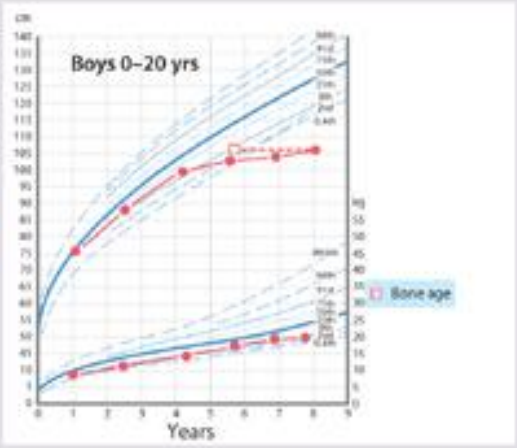
(c) Constitutional delay of growth and puberty → Short stature accentuated by delayed puberty. Delayed bone age

(d) Endocrine
- growth hormone deficiency
- hypothyroidism
- steroid excess
  - iatrogenic
  - Cushing syndrome
  - IGF-1 deficiency

→ Falling off height centiles. Weight centile >height centile. Short and overweight Markedly delayed bone age.





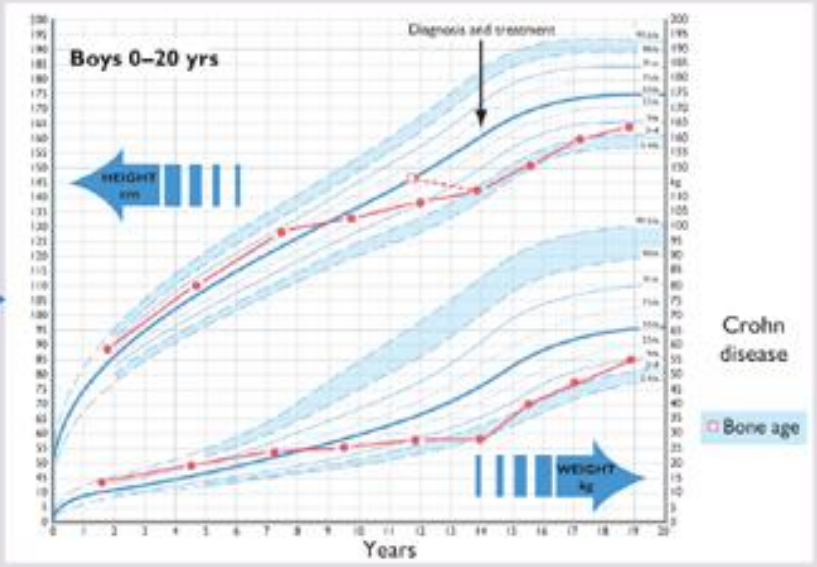


Causes & evaluation of short stature

(e)
Nutrition/ chronic illness
- gastrointestinal – coeliac, Crohn
- chronic renal failure

(f)
Psychosocial
- emotional deprivation/ neglect

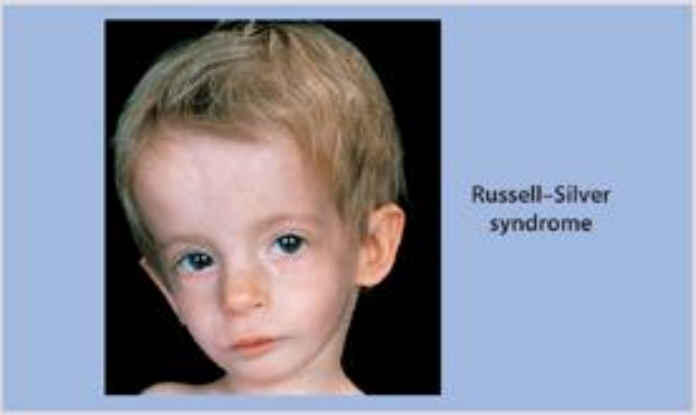
→ Falling off height centiles. Weight centile < height centile. Delayed bone age →



(g)
Syndromes
- Turner
- Noonan
- Down
- Russell–Silver

→ Dysmorphic features. Consider Turner syndrome in all short females →

(h)
Extreme short stature
→ Rare →



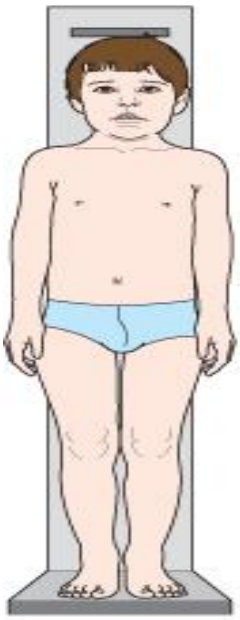
(i)
Disproportion
- sketelal dysplasia – legs>back
- storage disorders – back>legs

→

Table 11-1. Investigations considered for short stature

Investigation	Significance
X-ray of wrist and hand for bone age	Some delay in constitutional delay of growth and puberty
	Marked delay for hypothyroidism or growth hormone deficiency or other endocrine causes
Full blood count	Anaemia in coeliac or Crohn disease
Creatinine and electrolytes	Creatinine raised in chronic renal failure
Calcium, phosphate, alkaline phosphatise	Renal and bone disorders
Thyroid-stimulating hormone (TSH)	Raised in primary hypothyroidism
Karyotype	Turner syndrome shows 45XO, other chromosomal disorders
Endomysial and anti-tissue transglutaminase IgA antibodies	Usually present in coeliac disease
CRP (acute-phase reactant) and erythrocyte sedimentation rate (ESR)	Raised in Crohn disease
Growth hormone provocation tests (using insulin, glucagon, clonidine or arginine in specialist centres)	Growth hormone deficiency
IGF-1	Disorders of the growth hormone axis, including IGF-1 deficiency
0900 cortisol and dexamethasone suppression test	Cushing syndrome
MRI scan if neurological symptoms/signs	Craniopharyngioma or intracranial tumour
Limited skeletal survey	Skeletal dysplasia, scoliosis

Assessment of a child with short stature



Examination of the growth chart:
- Following growth centile lines for length/height, weight and head circumference?
  Consider familial, low birthweight, constitutional delay of growth and puberty, syndromes and skeletal dysplasias
- Growth failure with crossing of centile lines?
  Consider endocrine (including therapeutic corticosteroids), nutrition/chronic illness, psychosocial deprivation

Determine the mid-parental height
- For genetic target range

History
- Birth length, weight, head circumference and gestational age
- Pregnancy history: infection, intrauterine growth restriction, drug use, alcohol/smoking
- Feeding history
- Developmental milestones
- Family history of constitutional delay of growth and puberty or other diseases?
- Consanguinity pertaining to inherited conditions
- Features of chronic illness, endocrine causes, e.g. hypothyroidism, pituitary tumour, Cushing syndrome or psychosocial deprivation?
- Medications, e.g. corticosteroids?

Examination
- Dysmorphic features – chromosome/syndrome present?
  (But in Turner syndrome other stigmata may be absent)
- Chronic illness, e.g. Crohn, cystic fibrosis, coeliac disease?
- Evidence of endocrine causes?
- Disproportionate short stature from skeletal dysplasia?
- Pubertal stage?

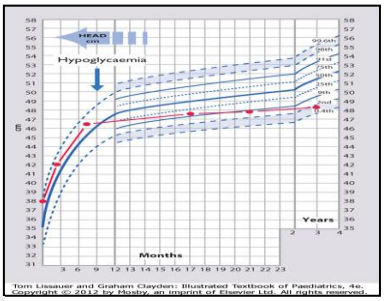
Diagnosis
Cause can usually be determined from the above and no tests are required

Table 11-2. Causes of excessive growth or tall stature

Familial	Most common cause
Obesity	Puberty is advanced, so final height centile is less than in childhood
Secondary	Hyperthyroidism
	Excess sex steroids - precocious puberty from whatever cause
	Excess adrenal androgen steroids - congenital adrenal hyperplasia
	True gigantism (excess GH secretion)
Syndromes	Long-legged tall stature:
	Marfan syndrome
	Homocystinuria
	Klinefelter syndrome (47 XXY and XXY karyotype)
	Proportionate tall stature at birth:
	Maternal diabetes
	Primary hyperinsulinism
	Beckwith syndrome
	Sotos syndrome - associated with large head, characteristic facial features and learnir

Case History 11.1 Microcephaly

Figure 11.10 shows the head circumference chart of Tim, who was healthy and was developing normally. At 9 months of age, he was rushed to hospital as he was unrousable from profound hypoglycaemia secondary to the deliberate administration of insulin by his mother, who had diabetes. Although Tim was taken into care and had no further hypoglycaemic episodes, his head circumference shows cessation of growth. He has developed moderate learning difficulties and mild cerebral palsy.



Box 11.1 Causes of a large head

- Tall stature
- Familial macrocephaly
- Raised intracranial pressure
- Hydrocephalus - progressive or arrested
- Chronic subdural haematoma
- Cerebral tumour
- Neurofibromatosis
- Cerebral gigantism (Sotos syndrome)
- CNS storage disorders, e.g. mucopolysaccharidosis (Hurler syndrome).

Abnormal head shape

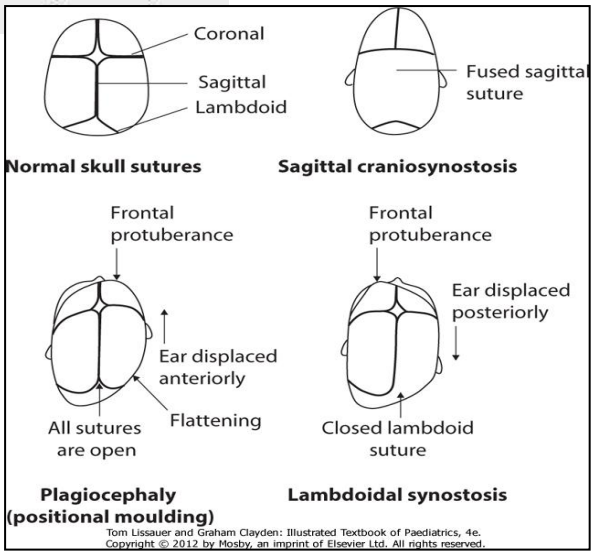
Box 11.2 Forms of craniosynostosis

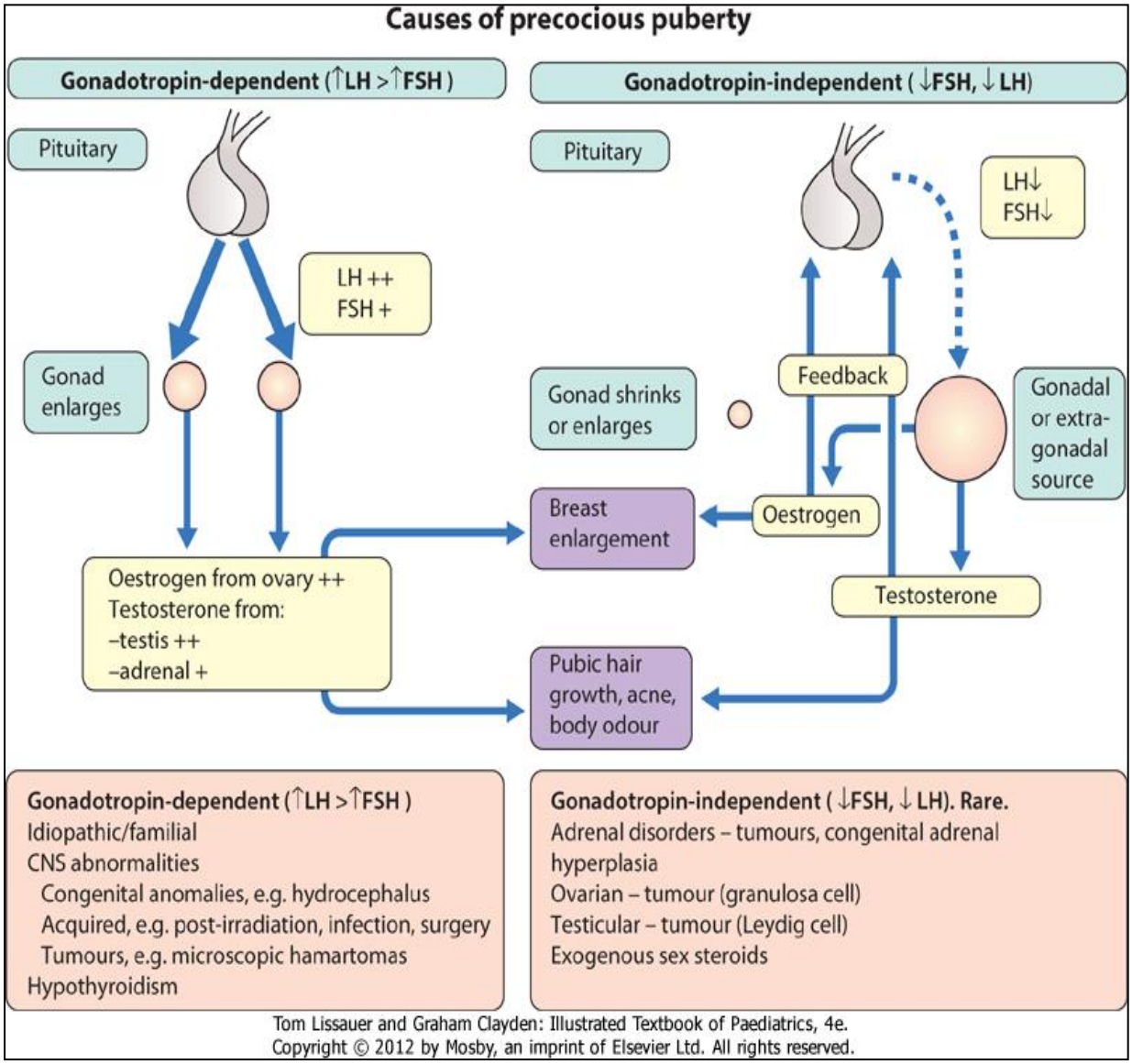
Localised

- Sagittal suture - long narrow skull
- Coronal suture - asymmetrical skull
- Lambdoid suture - flattening of skull

Generalised

- Multiple sutures resulting in microcephaly and developmental delay
- Genetic syndromes, e.g. with syndactyly in Apert syndrome, with exophthalmos in Crouzon syndrome.





Case history

11.2 precocious puberty in a boy

This 6-year-old boy presented with precocious puberty (Fig. 11.15a,b). He was noted to have multiple café-au-lait spots consistent with a diagnosis of neurofibromatosis type 1. An MRI scan showed a mass in the hypothalamus which proved to be an optic glioma. He was treated with radiotherapy, although full remission was not possible to achieve. The site of injection of gonadotropin super-agonist treatment to suppress his sexual development is covered by the plaster.

(b)

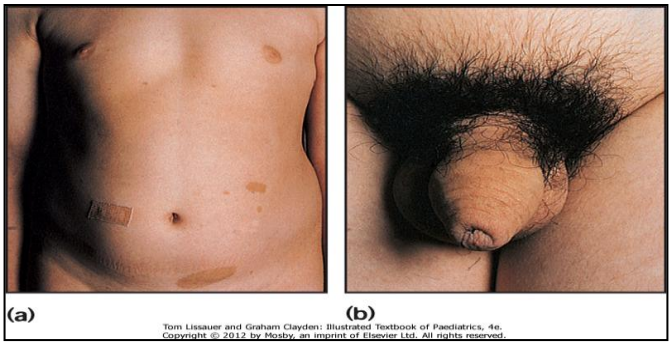


Figure 11.15 (a) Multiple café-au-lait spots. Neurofibromatosis type 1 was diagnosed. Genitalia showing stage 3 genitalia and pubic hair with 12 ml testicles bilaterally. He also had adult body odour.

Case History 11.3 Premature thelarche
This 18-month-old female developed enlargement of both breasts (Fig. 11.16). There was no pubic hair growth, sweatiness or body odour and her height was in the mid-parental range. Her bone age was only mildly advanced (21 months) and a pelvic ultrasound showed a prepubertal uterus, small volume ovaries with two cysts in the left ovary. Her subsequent growth rate was normal. A diagnosis of premature thelarche was made.

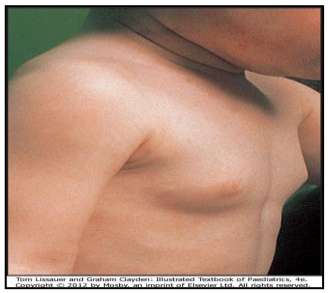


Figure 11.16 Premature breast development in an 18-month-old girl. The absence of a growth spurt and axillary and pubic hair differentiates it from precocious puberty. It is self-limiting and often resolves.

Box 11.3 Causes of delayed puberty
Constitutional delay of growth and puberty/familial

By far the commonest

Low gonadotropin secretion (hypogonadotropic hypogonadism)

- Systemic disease
  - - Cystic fibrosis, severe asthma, Crohn disease, organ failure, anorexia nervosa, starvation, excess physical training
- Hypothalamo-pituitary disorders
  - - Panhypopituitarism
  - - Isolated gonadotropin or growth hormone deficiency
  - - Intracranial tumours (including craniopharyngioma)
  - - Kallmann syndrome (LHRH deficiency and inability to smell)
- Acquired hypothyroidism

High gonadotropin secretion (hypergonadotropic hypogonadism)

- Chromosomal abnormalities
  - - Klinefelter syndrome (47 XXY)
  - - Turner syndrome (45 XO)
- Steroid hormone enzyme deficiencies
- Acquired gonadal damage
  - - Post-surgery, chemotherapy, radiotherapy, trauma, torsion of the testis, autoimmune disorder.

Chapter 12: Nutrition

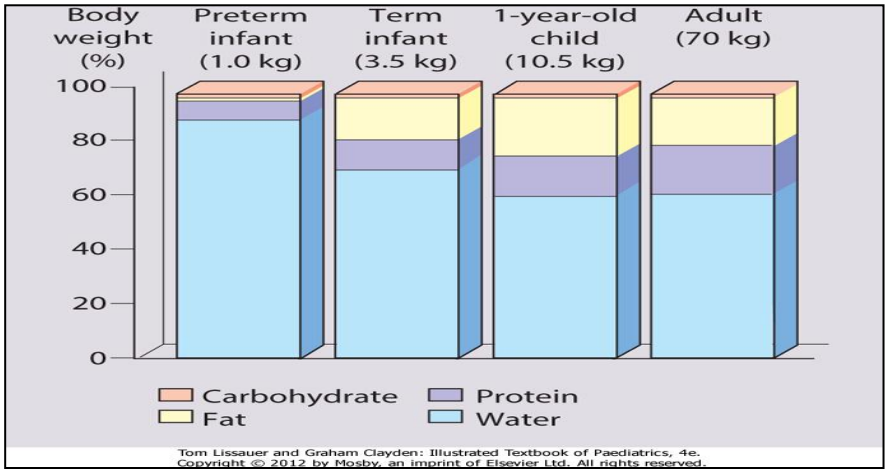


Figure 12.1 Body composition of preterm and term infants, children and adults. Newborn infants, particularly the preterm, have poor stores of fat and protein.

Table 12-1. Reference values for energy and protein requirements

Age	Energy (kcal/kg per 24 h)	Protein (g/kg per 24 h)
0-6 months	115	2.2
6-12 months	95	2.0
1-3 years	95	1.8
4-6 years	90	1.5
7-10 years	75	1.2
Adolescence	(male/female)	
11-14 years	65/55	1.0
15-18 years	60/40	0.8

Summary
Nutritional vulnerability

Infants are more vulnerable to poor nutrition because of:

- Poor stores of fat and protein
- Extra nutritional demands for growth - the weight of a term infant doubles by 4 months and trebles by 1 year.
- More frequent intercurrent illnesses that reduce food intake and increase nutritional demands.

Box 12.1 Why breast is best - the advantages of breast milk

Advantages of breast-feeding for the infant are that it:

- provides the ideal nutrition for infants during the first 4-6 months of life
- is life-saving in developing countries
- reduces the risk of gastrointestinal infection, and, in preterm infants, of necrotising enterocolitis
- enhances mother-child relationship
- reduces risk of insulin-dependent diabetes, hypertension and obesity in later life.

Advantages for the mother are that it:

- promotes close attachment between mother and baby
- increases the time interval between children, which is important in reducing birth rate in developing countries
- helps with a possible reduction in premenopausal breast cancer.

Box 12.2 Potential complications of breast-feeding

Unknown intake	Volume of milk intake not known
Transmission of infection	Maternal CMV, hepatitis B and HIV - increases risk of transmission to the baby
Breast-milk jaundice	Mild, self-limiting, unconjugated hyperbilirubinaemia; continue breast-feeding
Transmission of drugs	Antimetabolites and some other drugs contra-indicated. Check formulary
Nutrient inadequacies	Breast-feeding beyond 6 months without timely introduction of appropriate solids may lead to poor weight gain and rickets
Vitamin K deficiency	Insufficient vitamin K in breast milk to prevent haemorrhagic disease of the newborn. Supplementation is required
Potential transmission of environmental contaminants	Nicotine, alcohol, caffeine, etc.
Less flexible	Other family members cannot help or take part. More difficult in public places
Emotional upset	If difficulties or lack of success can be upsetting

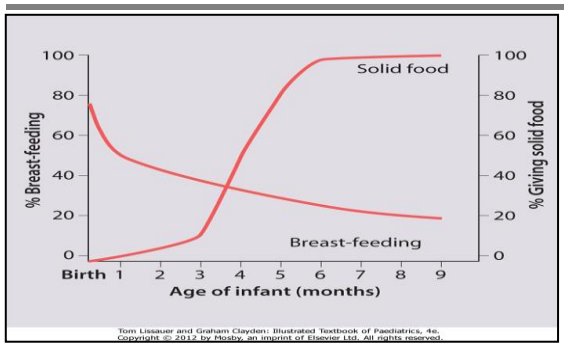


Figure 12.5 Prevalence of breast-feeding and proportion of infants given solid feeds during the first 9 months of life in the UK. Over the last 10 years there has been a marked increase in the prevalence of breast-feeding and delay in weaning onto solid food (Infant Feeding Survey, 2005)

Table 12-2. A comparison of human milk, cow's milk and infant formula (per 100 ml)

	Mature breast milk	Cow's milk	Infant formula (modified cow's milk)
Energy (kcal)	62	67	60-65
Protein (g)	1.3	3.5	1.5-1.9
Carbohydrate (g)	6.7	4.9	7.0-8.6
Casein : whey	40 : 60	63 : 37	40 : 60 to 63 : 37
Fat (g)	3.0	3.6	2.6-3.8
Sodium (mmol)	0.65	2.3	0.65-1.1
Calcium (mmol)	0.88	3.0	0.88-2.1
Phosphorus (mmol)	0.46	3.2	0.9-1.8
Iron (μmol)	1.36	0.9	8-12.5

Physiology of breast-feeding

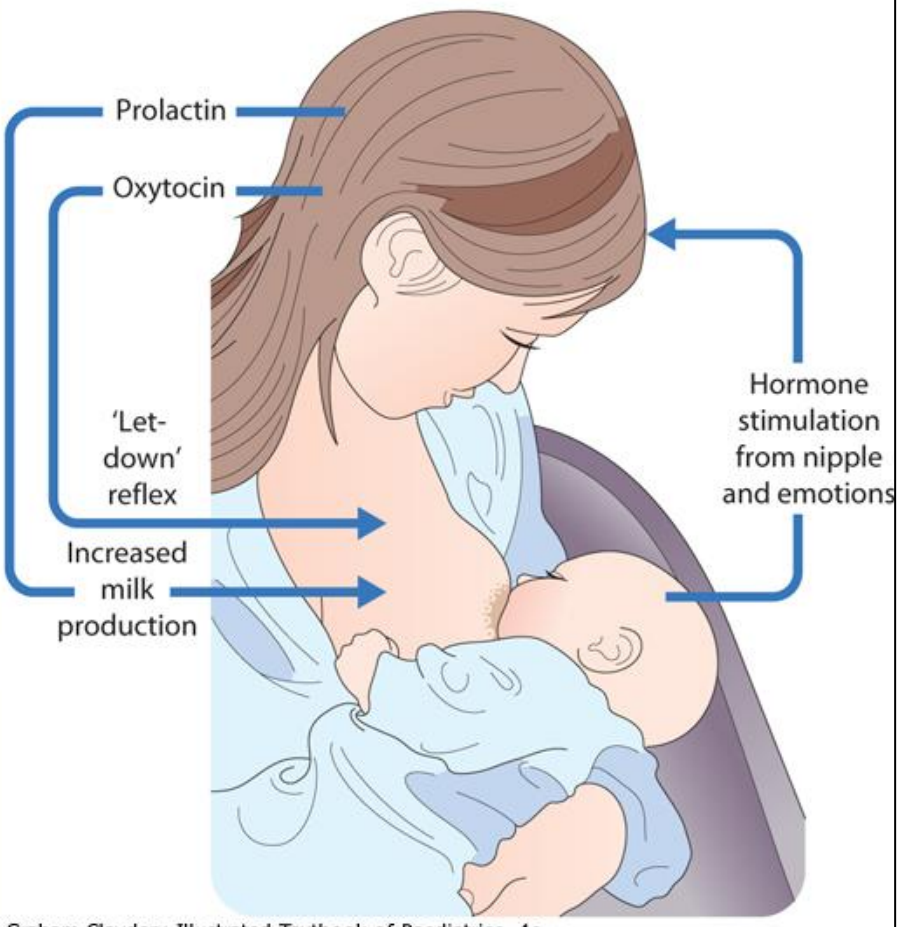
1. **Baby** uses rooting, sucking and swallowing reflexes to locate nipple and feed

2. **Tactile receptors** in nipple activated

3. **Hypothalamus** sends efferent impulses to anterior and posterior pituitary

4. **Anterior pituitary**
Prolactin secretion stimulates milk secretion by cuboidal cells in the acini of the breast

5. **Posterior pituitary**
Oxytocin secretion results in contraction of myoepithelial cells in the alveoli, forcing milk into larger ducts – the so-called 'let-down' reflex



Causes of failure to thrive

Causes	Examples
Inadequate intake	**Non-organic/enviromental** **Inadequate availability of food** • Feeding problems – insufficient breast milk or poor technique, incorrect preparation of formula • Insufficient or unsuitable food offered • Lack of regular feeding times • Infant difficult to feed – resists feeding or disinterested • Conflict over feeding, intolerance of normal feeding behaviour, e.g. messiness, throwing food around, leading to an early cessation of meals • Problems with budgeting, shopping, cooking food, famine • Low socioeconomic status **Psychosocial deprivation** • Poor maternal–infant interaction • Maternal depression • Poor maternal education **Neglect or child abuse** • Includes factitious illness: deliberate underfeeding to generate failure to thrive
Inadequate intake	**Organic** **Impaired suck/swallow** • Oro-motor dysfunction, neurological disorder, e.g. cerebral palsy • Cleft palate **Chronic illness leading to anorexia** • Crohn disease, chronic renal failure, cystic fibrosis, liver disease, etc.
Inadequate retention	Vomiting, severe gastro-oesophageal reflux
Malabsorption	Coeliac disease, cystic fibrosis, cow's milk protein intolerance, cholestatic liver disease, short gut syndrome, post-necrotising enterocolitis (NEC)
Failure to utilise nutrients	Syndromes Chromosomal disorders, e.g. Down syndrome, IUGR (intrauterine growth restriction) or extreme prematurity, congenital infection, metabolic disorders, e.g. congenital hypothyroidism, storage disorders, amino and organic acid disorders
Increased requirements	Thyrotoxicosis, cystic fibrosis, malignancy, chronic infection (HIV, immune deficiency) congenital heart disease, chronic renal failure

Box 12.3 Investigations to be considered in 'failure to thrive'

Investigation	Significance of an abnormality
Full blood count and differential white cell count	Anaemia, neutropenia, lymphopenia (immune deficiency)
Serum creatinine urea, electrolytes, acid-base status, calcium, phosphate	Renal failure, renal tubular acidosis, metabolic disorders, William syndrome
Liver function tests	Liver disease, malabsorption, metabolic disorders
Thyroid function tests	Hypothyroidism or hyperthyroidism
Acute phase reactant, e.g. C-reactive protein	Inflammation
Ferriaztin	Iron deficiency anaemia
Immunoglobulins	Immune deficiency
IgA tissue transglutaminase antibodies	Coeliac disease
Urine microscopy, culture and dipsticks	Urinary tract infection, renal disease
Stool microscopy, culture and elastase	Intestinal infection, parasites, elastase decreased in pancreatic insufficiciency
Karyotype in girls	Turner syndrome
Chest X-ray and sweat test	Cystic fibrosis

Summary
Failure to thrive

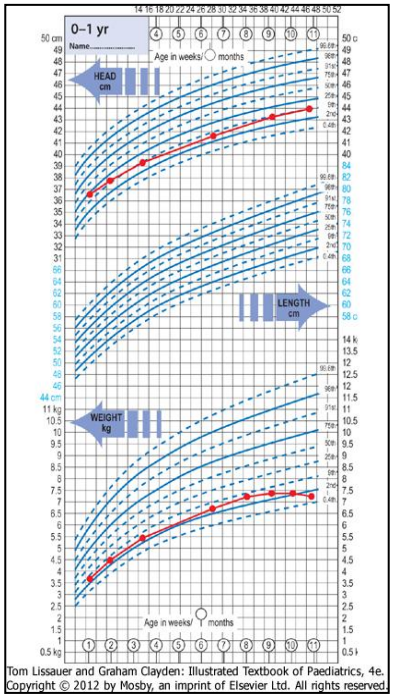
- is a description, not a diagnosis
- weights of infants are only helpful if accurate and plotted on a centile chart
- is present if an infant's weight falls across two centile lines
- is likely to be present the further the weight is below the 2nd centile
- is mostly due to inadequate food intake
- is accompanied by abnormal symptoms or signs if there is organic disease
- most affected infants and toddlers do not require any investigations and are managed in primary care by increasing energy intake by dietary and behavioural modification and monitoring growth.

Case history 12.1 Non-organic FTT

Jamie, aged 11 months, was causing concern to his health visitor as he was not putting on any weight (Fig. 12.9). She arranged for him to be assessed by his general practitioner, who found that he was otherwise well. His mother was a single parent who left school at 16 years and had Jamie at the age of 18. They lived in a high-rise flat and Jamie's mother received income support. Her own mother lived on the other side of the city.

On visiting the home, the health visitor found Jamie's mother to be tense and anxious. In particular, she was worried about making ends meet. She fed Jamie the same food as she ate herself, together with pasteurised milk, which she had started at 6 months of age. The meals were chaotic. After a few mouthfuls, Jamie stopped eating and his mother did not coax him but became frustrated and angry.

Jamie's health visitor suggested strategies for increasing Jamie's food intake (Box 12.4). She continued to provide support and encouragement to his mother and arranged a nursery placement for Jamie. By 2 years of age, he had caught up by one centile line, but still ate erratically.



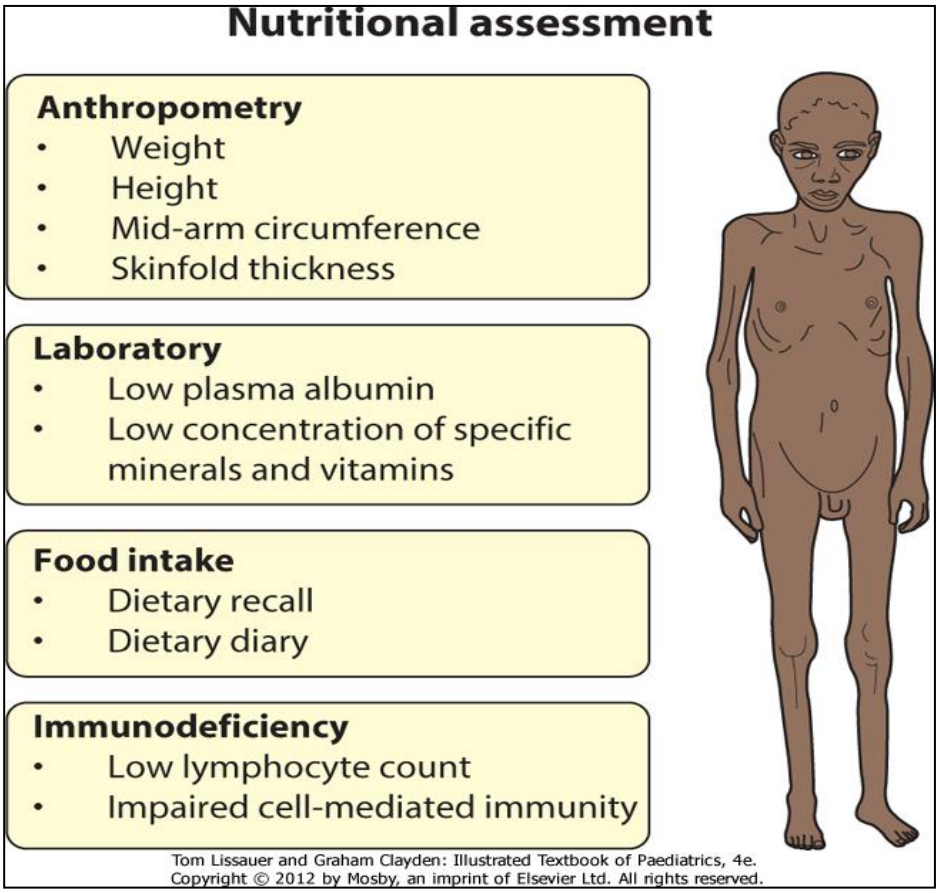
Box 12.4 Strategies for increasing energy intake

Dietary

- Three meals and two snacks each day
- Increase number and variety of foods offered
- Increase energy density of usual foods (e.g. add cheese, margarine and cream)
- Decrease fluid intake, particularly squash

Behavioural

- Have meals at regular times, eaten with other family members
- Praise when food is eaten
- Gently encourage child to eat, but avoid conflict
- Never force-feed.



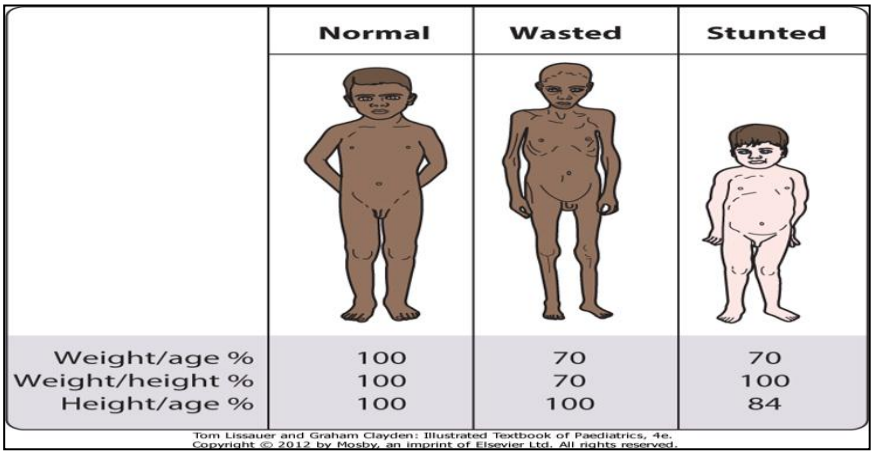


Figure 12.11 Comparison of a normal, wasted and stunted child at 1 year. Low weight for height reveals a child of normal height, but who is thin and wasted, whereas low height for age reveals a short, non-wasted child.

Summary
Malnutrition

- Worldwide - contributes to about a third of all childhood deaths; often a consequence of war and social disruption, as well as famine and natural disasters
- In developed countries - results from poverty, parental neglect or poor education, restrictive diets, children with feeding disorders or chronic illness or anorexia nervosa
- Can be identified by anthropometric measurement; laboratory tests are not usually required
- Marasmus - weight for height more than 3 Standard Deviations below the median; wasted, wizened appearance; apathetic
- Kwashiorkor - generalised oedema, sparse and depigmented hair, skin rash, angular stomatitis, distended abdomen and enlarged liver, diarrhoea.

Box 12.5 Causes of rickets

Nutritional (primary) rickets - risk factors

- Living in northern latitudes
- Dark skin
- Decreased exposure to sunlight, e.g. in some Asian children living in the UK
- Maternal vitamin D deficiency
- Diets low in calcium, phosphorus and vitamin D, e.g. exclusive breast-feeding into late infancy or, rarely, toddlers on unsupervised 'dairy-free' diets
- Macrobiotic, strict vegan diets
- Prolonged parenteral nutrition in infancy with an inadequate supply of parenteral calcium and phosphate

Intestinal malabsorption

- Small bowel enteropathy (e.g. coeliac disease)
- Pancreatic insufficiency (e.g. cystic fibrosis)
- Cholestatic liver disease
- High phytic acids in diet (e.g. chapattis)

Defective production of $25(OH)D_2$

- Chronic liver disease

Increased metabolism of $25(OH)D_3$

- Enzyme induction by anticonvulsants (e.g. phenobarbital)

Defective production of $1,25(OH)_2D_3$

- Hereditary type I vitamin D-resistant (or dependent) rickets (mutation which abolishes activity of renal hydroxylase)
- Familial (X-linked) hypophosphataemic rickets (renal tubular defect in phosphate transport)
- Chronic renal disease
- Fanconi syndrome (renal loss of phosphate)

Target organ resistance to $1,25(OH)_2D_3$

- Hereditary vitamin D-dependent rickets type II (due to mutations in vitamin D receptor gene).

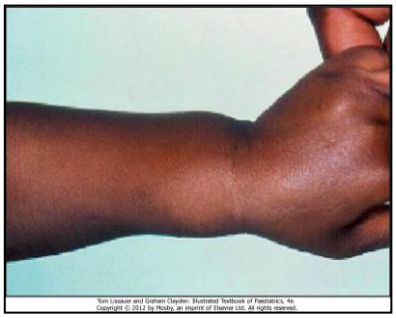
Box 12.6 Clinical features of rickets

- Misery
- Failure to thrive/short stature
- Frontal bossing of skull
- Craniotabes
- Delayed closure of anterior fontanelle
- Delayed dentition
- Rickety rosary
- Harrison sulcus (Fig. 12.16)
- Expansion of metaphyses (especially wrist)
- Bowing of weight-bearing bones
- Hypotonia
- Seizures (late).

Case History 12.2 Seizures and rickets

Mohammed, a 13-month-old Somalian boy, was admitted to the A&E department with a generalised afebrile seizure. This was initially controlled with per rectum diazepam. Some 20 minutes later he had another generalised seizure and needed intravenous anticonvulsant to control his seizure.

His mother said that he was a healthy child. He was born at term, birthweight 3.1 kg, and was still breast-fed. Some weaning foods were started at 7-8 months, but he preferred feeding at the breast. He had only recently begun to sit without support.



His weight and head circumference were on the 2nd-9th centile. He had marked frontal bossing, widened wrist (Fig. 12.17) and other epiphyses, Harrison sulci, wide anterior fontanelle, craniotabes and a rachitic rosary. He would not take his weight on standing.

Investigations showed a low calcium and phosphate level, a high alkaline phosphatase and parathyroid hormone level and a very low vitamin D level, confirming rickets. Liver and renal function tests were normal and coeliac screen was negative. His wrist X-ray showed characteristic features (Fig. 12.18). A detailed dietetic history revealed a diet deficient in calcium and vitamin D, confirming nutritional rickets as the cause.

Dietetic input was provided. He was started on oral vitamin D and his solid food intake was increased to ensure that he was receiving sufficient calcium and vitamin D in his diet. His rickets resolved.

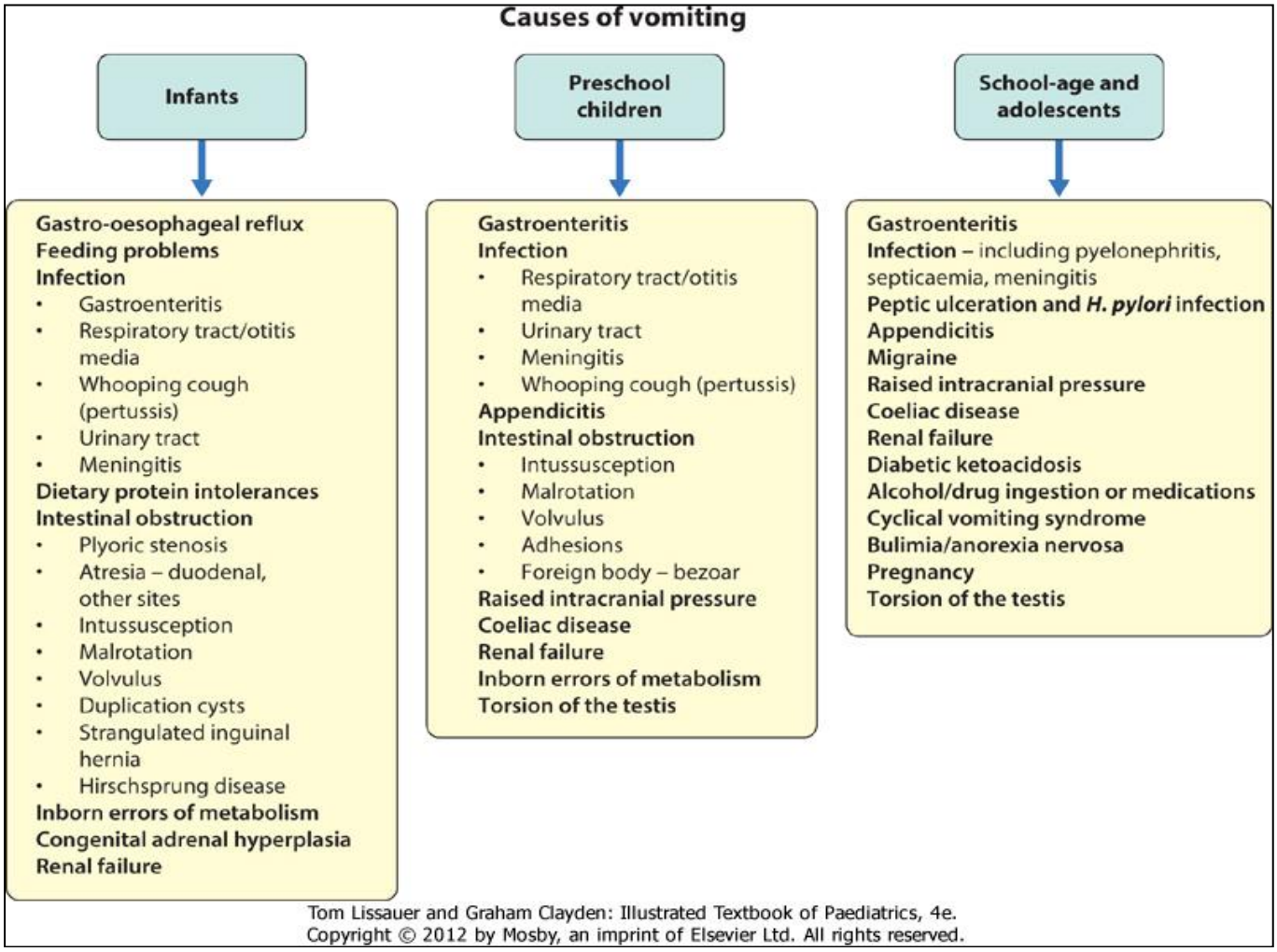
Summary
Rickets

- Nutritional - has re-emerged in the UK in Asian and black infants exclusively breast-fed into late infancy
- Diagnosis - serum calcium is low or normal, phosphorus low, plasma alkaline phosphatase greatly increased, 25-hydroxyvitamin D low and parathyroid hormone elevated
- X-ray features - cupping and fraying of the metaphyses and widened epiphyseal plate.

Chapter 13: Gastroenterology

Box 13.1 'Red Flag' clinical features in the vomiting child

Bile-stained vomit	Intestinal obstruction
Haematemesis	Oesophagitis, peptic ulceration, oral/nasal bleeding
Projectile vomiting, in first few weeks of life	Pyloric stenosis
Vomiting at the end of paroxysmal coughing	Whooping cough (pertussis)
Abdominal tenderness/abdominal pain on movement	Surgical abdomen
Abdominal distension	Intestinal obstruction, including strangulated inguinal hernia
Hepatosplenomegaly	Chronic liver disease
Blood in the stool	Intussusception, gastroenteritis - salmonella or campylobacter
Severe dehydration, shock	Severe gastroenteritis, systemic infection (urinary tract infection, meningitis), diabetic ketoacidosis
Bulging fontanelle or seizures	Raised intracranial pressure
Failure to thrive	Gasto-oesophageal reflux, coeliac disease and other chronic gastrointestinal conditions



Summary
Vomiting in infants

- Common chronic causes are gastro-oesophageal reflux and feeding problems, e.g. force-feeding or overfeeding
- If transient, with other symptoms, e.g. fever, diarrhoea or runny nose and cough, most likely to be gastroenteritis or respiratory tract infection, but consider urine infection and meningitis
- If projectile at 2-7 weeks of age, exclude pyloric stenosis
- If bile stained, exclude intestinal obstruction, especially intussusception, malrotation and a strangulated inguinal hernia. Assess for dehydration and shock.

Box 13.2 Complications of gastro-oesophageal reflux

- Failure to thrive from severe vomiting
- Oesophagitis - haematemesis, discomfort on feeding or heartburn, iron deficiency anaemia
- Recurrent pulmonary aspiration - recurrent pneumonia, cough or wheeze, apnoea in preterm infants
- Dystonic neck posturing (Sandifer syndrome)
- Apparent life-threatening events (ALTE)

Case History 13.1 Severe gastro-oesophageal reflux
This infant (Fig. 13.2a) had a history of frequent regurgitation from the first few days of life. He developed two chest infections. Some of the vomits contained altered blood. A 24-hour oesophageal pH study showed severe gastro-oesophageal reflux (Fig. 13.2b,c). Endoscopy showed oesophagitis. He had probably had episodes of aspiration pneumonia. Symptoms resolved on treatment with feed thickeners and omeprazole. His parents also commented on how much better he slept at night. Treatment was reduced from 14 months of age and the symptoms did not recur.

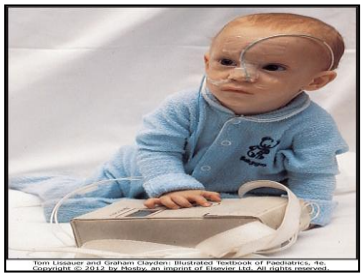


Figure 13.2a A pH sensor has been placed in the lower oesophagus.

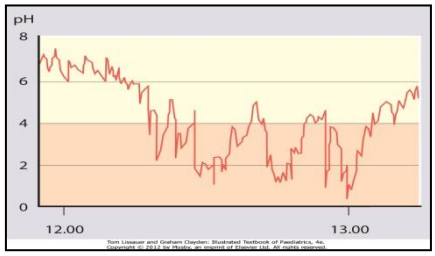


Figure 13.2b A section of the 24-hour oesophageal pH study showing severe reflux, with frequent drops in pH below 4

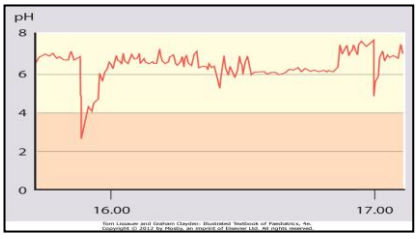


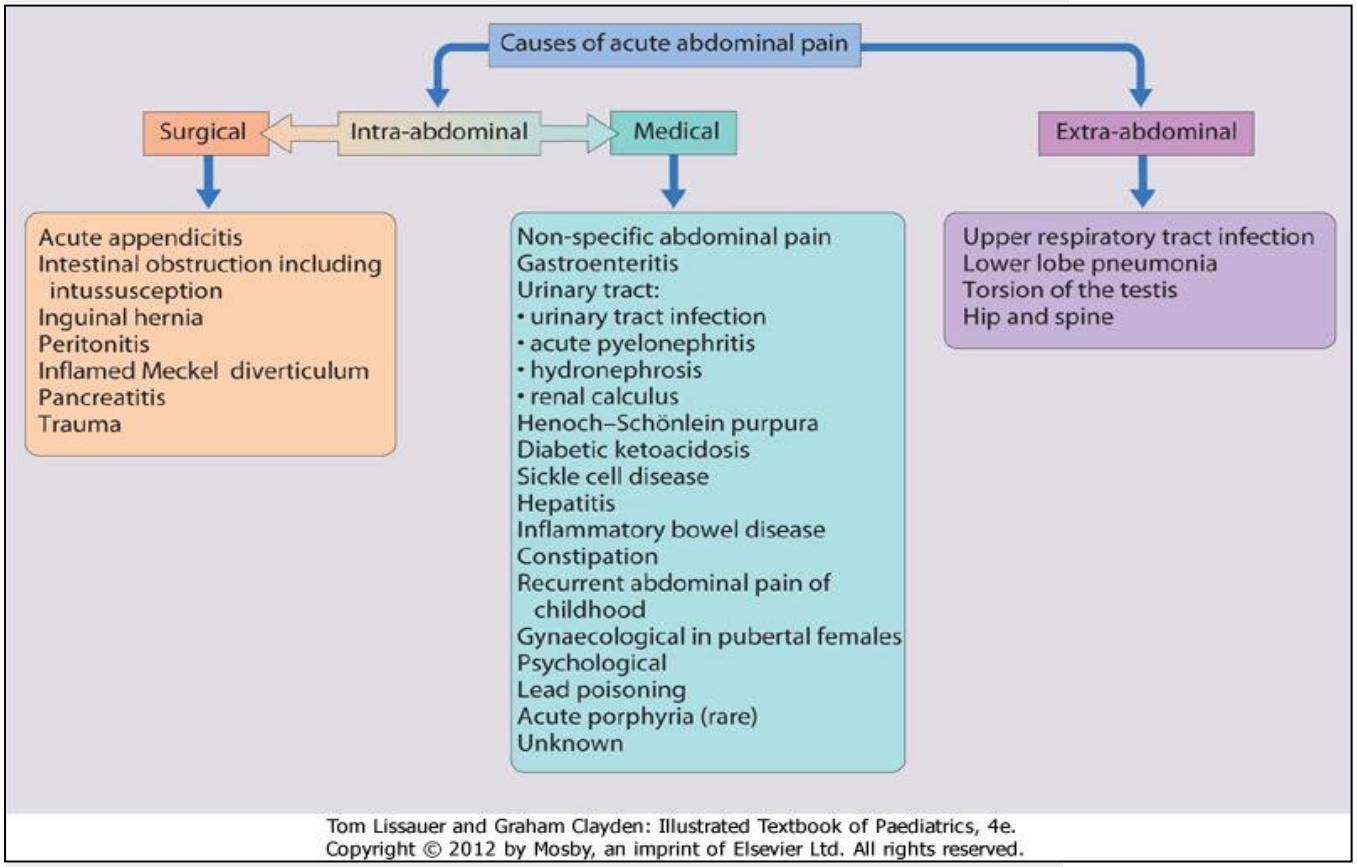
Figure 13.2c A section of a normal oesophageal pH study. The lower oesophageal pH is above 4 for most of the time

Summary
Gastro-oesophageal reflux

- Occurs in otherwise normal infants, but risk is increased if neuromuscular problems or surgery to the oesophagus or diaphragm
- Is treated if troublesome with upright positioning, feed thickening, medication and sometimes fundoplication
- Investigations are performed if diagnosis is unclear or complications occur.

Summary
Pyloric stenosis

- More common in boys and those with a maternal family history
- Signs are: visible gastric peristalsis, palpable abdominal mass on test feed and possible dehydration
- Associated with hyponatraemia, hypokalaemia and hypochloraemic alkalosis
- Diagnosis may be confirmed by ultrasound
- Treated by surgery after rehydration and correction of electrolyte imbalance.



Summary
Acute abdominal pain in older children and adolescents

- Exclude medical causes, in particular lower lobe pneumonia, diabetic ketoacidosis, hepatitis, pyelonephritis
- Check for strangulated inguinal hernia or torsion of the testis in boys
- On palpating the abdomen in children with acute appendicitis, guarding and rebound tenderness are often absent or unimpressive, but pain from peritoneal inflammation may be demonstrated on coughing, walking or jumping
- To distinguish between acute appendicitis and non-specific abdominal pain may require close monitoring and repeated evaluation in hospital.

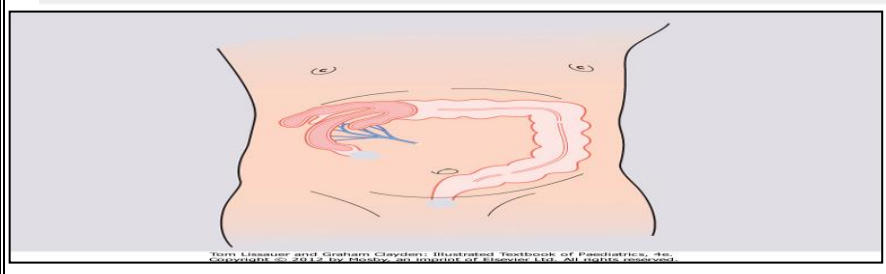


Figure 13.6a Intussusception, showing why the blood supply to the gut rapidly becomes compromised, making relief of this form of obstruction urgent.

Summary
Intussusception

- Usually occurs between 3 months and 2 years of age
- Clinical features are paroxysmal, colicky pain with pallor, abdominal mass, redcurrant jelly stool
- Shock is an important complication and requires urgent treatment
- Reduction is attempted by rectal air insufflation unless peritonitis is present
- Surgery is required if reduction with air is unsuccessful or for peritonitis.

Summary
Meckel diverticulum

- Occurs in 2% of individuals.
- Generally asymptomatic, but may present with bleeding (which may be life-threatening), intussusception, volvulus or diverticulitis.
- Treatment is by surgical resection.

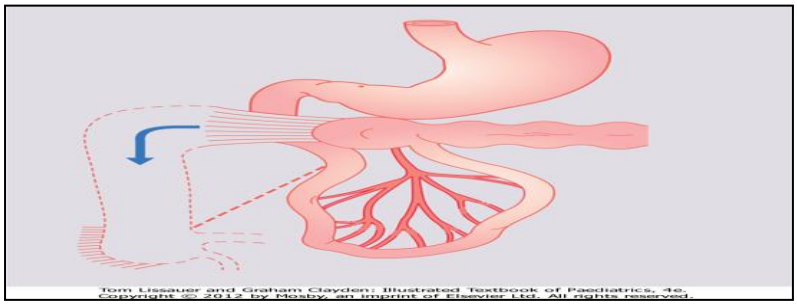


Figure 13.8 The commonest form of malrotation, with the caecum remaining high and fixed to the posterior abdominal wall. There are Ladd bands obstructing the duodenum. Dotted lines show normal anatomy.

Summary
Malrotation

- Uncommon but important to diagnose
- Usually presents in the first 1-3 days of life with intestinal obstruction from Ladd bands obstructing the duodenum or volvulus
- May present at any age with volvulus causing obstruction and ischaemic bowel
- Clinical features are bilious vomiting, abdominal pain and tenderness from peritonitis or ischaemic bowel
- An urgent upper gastrointestinal contrast study is indicated if there is bilious vomiting
- Treatment is urgent surgical correction.

Symptoms and signs that suggest organic disease:

- Epigastric pain at night, haematemesis (duodenal ulcer)
- Diarrhoea, weight loss, growth failure, blood in stools (inflammatory bowel disease)
- Vomiting (pancreatitis)
- Jaundice (liver disease)
- Dysuria, secondary enuresis (urinary tract infection)
- Bilious vomiting and abdominal distension (malrotation)

Summary

Causes and assessment of the child with recurrent abdominal pain

>90% no structural cause identified

Gastrointestinal
- Irritable bowel syndrome
- Constipation
- Non-ulcer dyspepsia
- Abdominal migraine
- Gastritis and peptic ulceration
- Inflammatory bowel disease
- Malrotation

Gynaecological
- Dysmenorrhoea
- Ovarian cysts
- Pelvic inflammatory disease

Psychosocial – bullying, abuse, stress, etc. – a small proportion

Hepatobility/pancreatic
- Hepatitis
- Gall stones
- Pancreatitis

Urinary tract
- Urinary tract infection
- Pelvi-ureteric junction (PUJ) obstruction

Box 13.3 Conditions which can mimic gastroenteritis

Systemic infection	Septicaemia, meningitis
Local infections	Respiratory tract infection, otitis media, hepatitis A, urinary tract infection
Surgical disorders	Pyloric stenosis, intussusception, acute appendicitis, necrotising enterocolitis, Hirschsprung disease
Metabolic disorder	Diabetic ketoacidosis
Renal disorder	Haemolytic uraemic syndrome
Other	Coeliac disease, cow's milk protein intolerance, adrenal insufficiency

Table 13-1. Clinical assessment of dehydration

	No clinical dehydration	Clinical dehydration	Shock
General appearance	Appears well	Appears unwell or deteriorating	Appears unwell or deteriorating
Conscious level	Alert and responsive	Altered responsiveness, e.g. irritable, lethargic	Decreased level of consciousness
Urine output	Normal	Decreased	Decreased
Skin colour	Normal	Normal	Pale or mottled
Extremities	Warm	Warm	Cold
Eyes	Normal	Sunken	Grossly sunken
Mucous membranes	Moist	Dry	Dry
Heart rate	Normal	Tachycardia	Tachycardia
Breathing	Normal	Tachypnoea	Tachypnoea
Peripheral pulses	Normal	Normal	Weak
Capillary refill time	Normal	Normal	Prolonged (>2 s)
Skin turgor	Normal	Reduced	Reduced
Blood pressure	Normal	Normal	Hypotension (indicates decompensated shock)

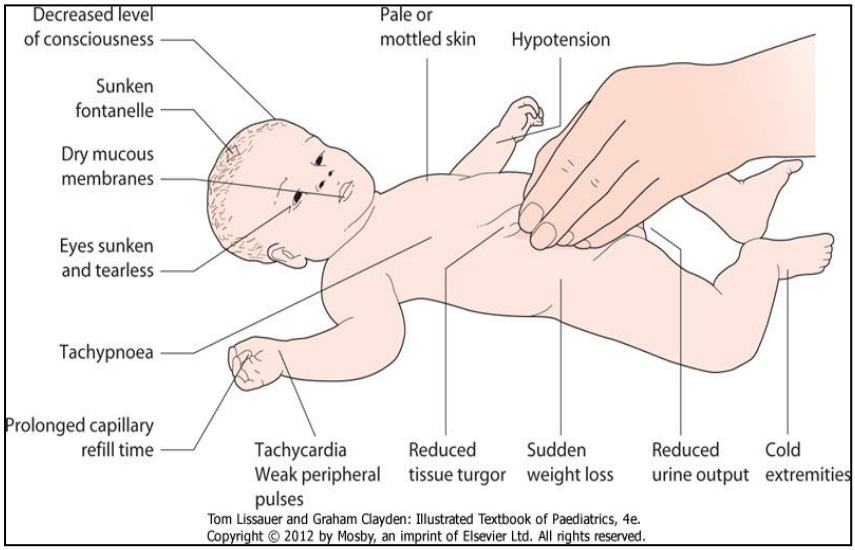
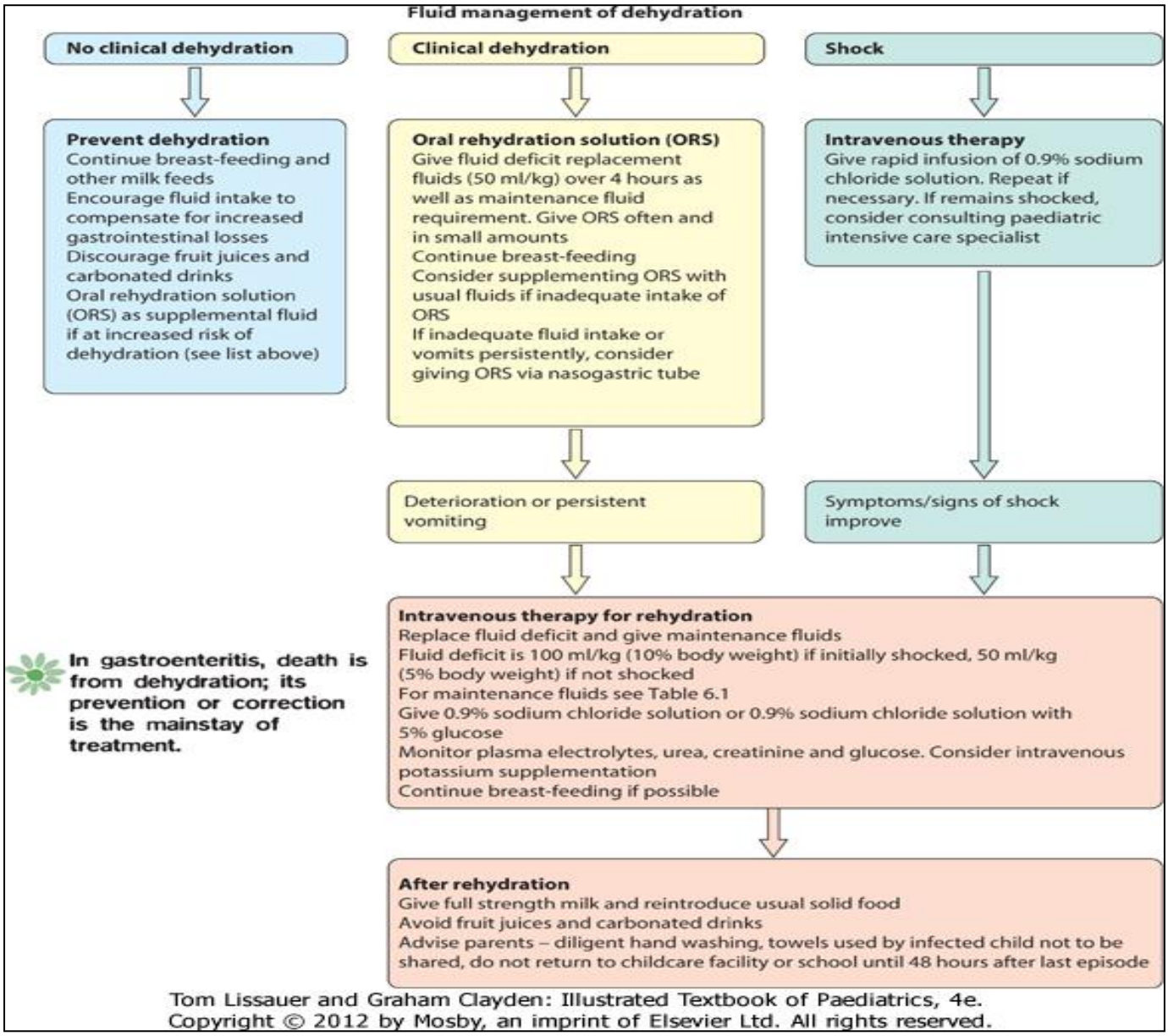


Figure 13.9 Clinical features of shock from dehydration in an infant.



Summary
Gastroenteritis

Gastroenteritis in developing countries:

- results in death from dehydration of hundreds of thousands of children worldwide every year
- is mostly bacterial from contaminated drinking water and food
- oral rehydration solution - saves the lives of millions of children worldwide each year.

Gastroenteritis in developed countries:

- is mostly viral, but it can be caused by *Campylobacter*, *Shigella* and *Salmonella*
- infants are particularly susceptible to dehydration
- dehydration is assessed as no clinical dehydration, clinical dehydration or shock according to symptoms and signs, but clinical assessment of severity is problematic
- oral rehydration solution is effective in most, but intravenous fluid is required for shock, ongoing vomiting or clinical deterioration.

Chapter 14: Infections

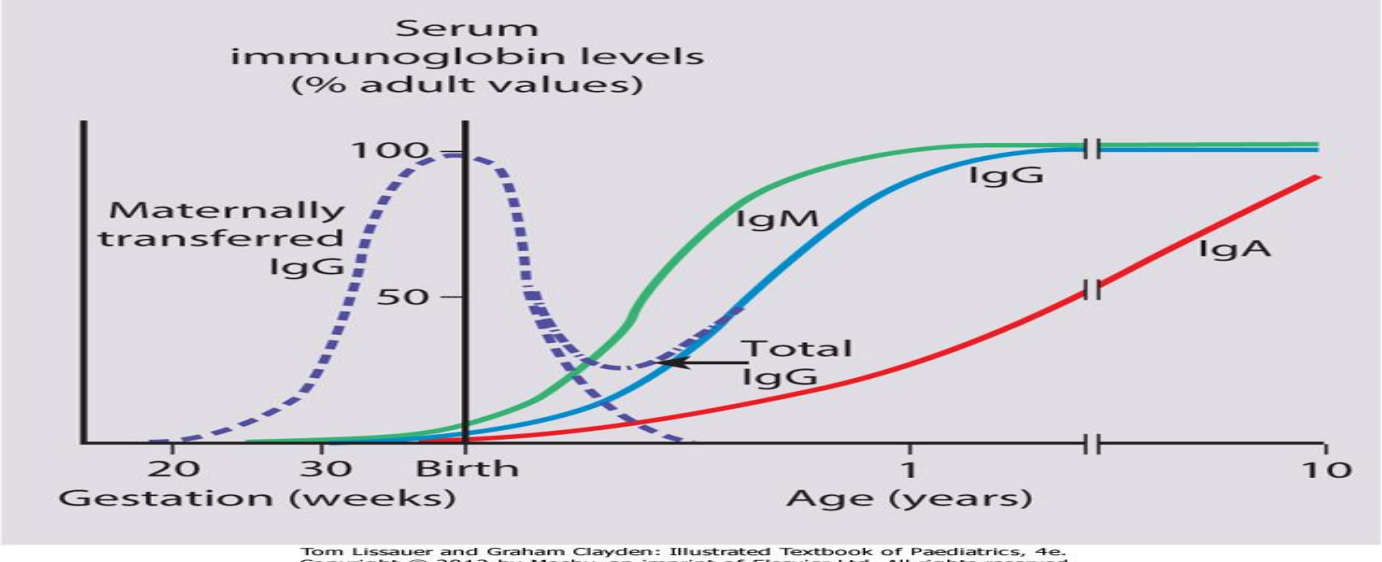
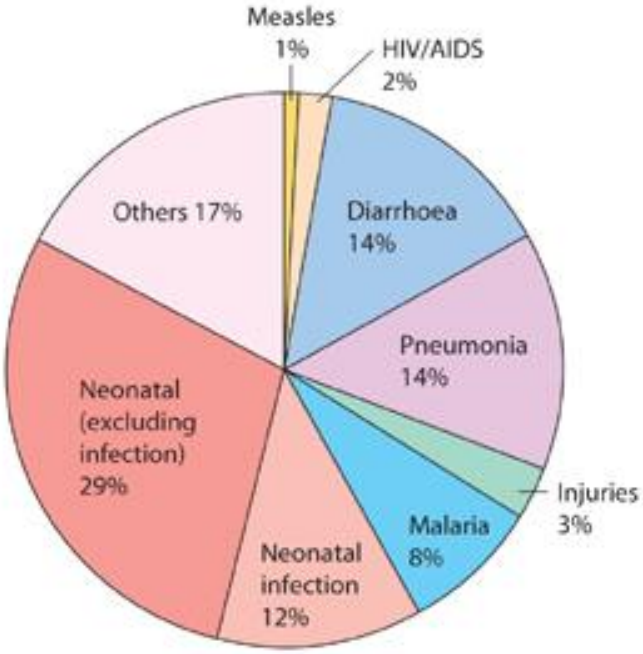


Figure 14.2 Serum immunoglobulin levels in the fetus and infant. When maternal immunoglobulin levels decline, infants become susceptible to viral infections.

Worldwide causes of death in children < 5 years old



Malaria
- Deaths mostly from cerebral malaria from *Plasmodium falciparum* in Sub-Saharan Africa
- Deaths have been reduced in many countries by insecticide-treated bed nets and early treatment with artemisinin-based combination therapy

Diarrhoea
- Most <2 years old
- Often bacterial, although rotavirus also a major cause globally
- Results in undernutrition, poor growth, death
- Usually treated with oral rehydration solution, continuing to breast-feed
- Antibiotics only for cholera, dysentery, giardiasis, amoebiasis

Pneumonia
- Risk factors – low birthweight, young age, not breast-fed, vitamin A deficiency, overcrowding
- Predominantly bacterial
- Strategy to reduce mortality:
  - Prevention – breast feeding and hand hygiene
  - Prevention – immunisation
  - Treatment – effective case management by early diagnosis using WHO guidelines (fever, cough, tachypnoea, chest recession, head nodding) and prompt treatment with antibiotics

Measles
- Preventable by immunisation

Neonatal infection
- Remains major cause of death
- Mainly early-onset infection acquired at delivery

• **Every year, over half of the 8.8 million deaths of children <5 years old is from infections**

Box 14.1 Septic screen

- Blood culture
- Full blood count including differential white cell count
- Acute phase reactant, e.g. C-reactive protein (CRP)
- Urine sample

Consider if indicated

- Chest X-ray
- Lumbar puncture (unless contraindicated)
- Rapid antigen screen on blood/CSF/urine
- Meningococcal and pneumococcal PCR on blood/CSF
- PCR for viruses in CSF (especially HSV and enterovirus).

Summary
The febrile child

- Upper respiratory tract infection (URTI) is an extremely common cause
- Check for otitis media
- Serious bacterial infection must be considered if there is no focus of infection, especially urinary tract infection or septicaemia, or there are Red Flag features of life-threatening illness
- The younger the child, the lower the threshold for performing a septic screen and starting antibiotics.

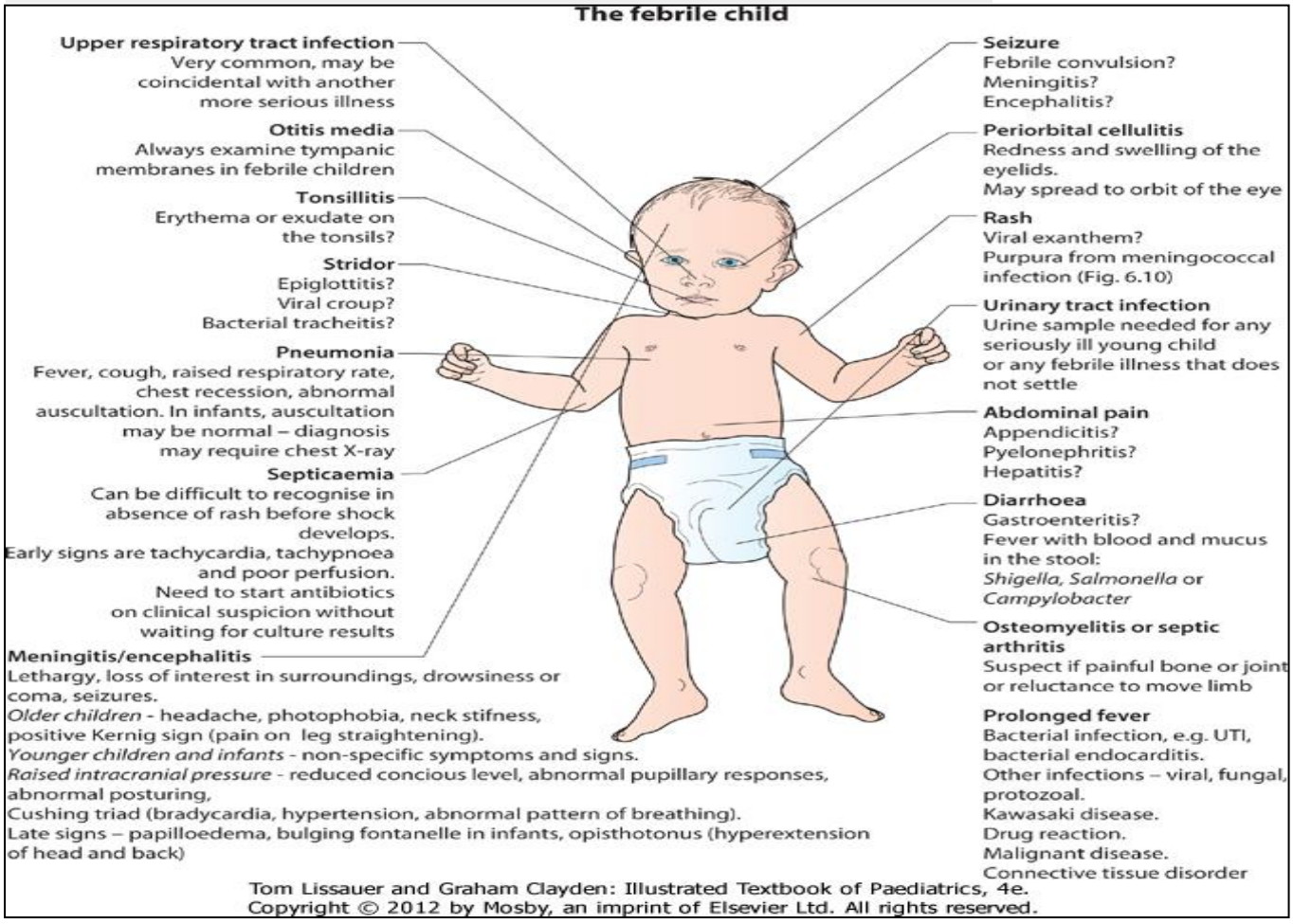


Figure 14.3 Some diagnostic clues to evaluating the febrile child.

Table 14-1. Organisms causing bacterial meningitis according to age

Neonatal-3 months	Group B streptococcus
	E. coli and other coliforms
	Listeria monocytogenes
1 month-6 years	*Neisseria meningitidis*
	Streptococcus pneumoniae
	Haemophilus influenzae
>6 years	*Neisseria meningitidis*
	Streptococcus pneumoniae

Assessment & investigation of meningitis/encephalitis

History
- Fever
- Headache
- Photophobia
- Lethargy
- Poor feeding/vomiting
- Irritability
- Hypotonia
- Drowsiness
- Loss of consciousness
- Seizures

Examination
- Fever
- Purpuric rash (meningococcal disease)
- Neck stiffness (not always present in infants)
- Bulging fontanelle in infants
- Opisthotonus (arching of back)
- Positive Brudzinski/Kernig signs
- Signs of shock
- Focal neurological signs
- Altered conscious level
- Papilloedema (rare)

Investigations
- Full blood count and differential count
- Blood glucose and blood gas (for acidosis)
- Coagulation screen, C-reactive protein
- Urea and electrolytes, liver function tests
- Culture of blood, throat swab, urine, stool for bacteria and viruses
- Rapid antigen test for meningitis organisms (can be done on blood, CSF, or urine)
- Lumbar puncture for CSF unless contraindicated (see below for tests on CSF)
- Serum for comparison of convalescent titres
- PCR of blood and CSF for possible organisms
- If TB suspected: chest X-ray, Mantoux test, gastric washings or sputum, early morning urines
- Consider CT/MRI brain scan and EEG

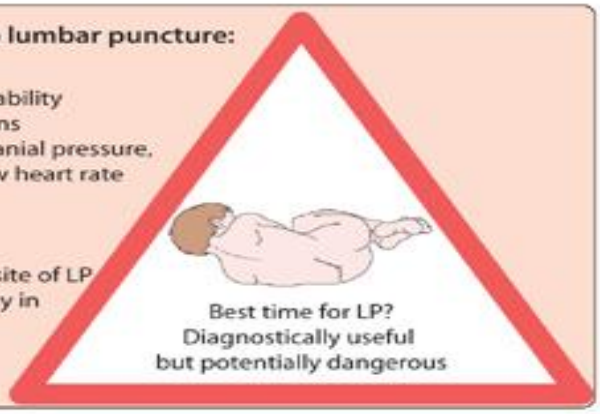
Signs associated with neck stiffness

Brudzinski sign – flexion of the neck with the child supine causes flexion of the knees and hips

Kernig sign – with the child lying supine and with the hips and knees flexed, there is back pain on extension of the knee

Contraindications to lumbar puncture:

- Cardiorespiratory instability
- Focal neurological signs
- Signs of raised intracranial pressure, e.g. coma, high BP, low heart rate or papilloedema
- Coagulopathy
- Thrombocytopenia
- Local infection at the site of LP
- If it causes undue delay in starting antibiotics



Typical changes in the CSF in meningitis or encephalitis, beyond the neonatal period

	Aetiology	Appearance	White blood cells	Protein	Glucose
Normal	—	Clear	0–5/mm^3	0.15–0.4 g/L	≥50% of blood
Meningitis	Bacterial	Turbid	Polymorphs:↑↑	↑↑	↓↓
	Viral	Clear	Lymphocytes:↑ (initially may be polymorphs)	Normal/↑	Normal/↓
	Tuberculosis	Turbid/clear/ viscous	Lymphocytes:↑	↑↑↑	↓↓↓
Encephalitis	Viral/unknown	Clear	Normal/↑ lymphocytes	Normal/↑	Normal/↓

Summary
Meningitis

- Predominantly a disease of infants and children
- Incidence has been reduced by immunisation
- Clinical features: non-specific in children under 18 months - fever, poor feeding, vomiting, irritability, lethargy, drowsiness, seizures or reduced consciousness; late signs - bulging fontanelle, neck stiffness and arched back (opisthotonos)
- Septicaemia can kill in hours; good outcome requires prompt resuscitation and antibiotics
- Any febrile child with a purpuric rash should be given intramuscular benzylpenicillin immediately and transferred urgently to hospital.

Summary
Encephalitis

- Onset can be insidious and includes behavioural change
- Consider if HSV (herpes simplex virus) could be the cause
- Treat potential HSV with parenteral high-dose aciclovir until diagnosis is excluded.

Case History 14.1 Meningococcal septicaemia
This 7-month-old boy presented with a 12-hour history of lethargy and a spreading purpuric rash. In hospital, he required immediate resuscitation and transfer to a paediatric intensive care unit for multi-organ failure (Fig. 14.7a). The gross oedema is from leak of capillary fluid into the tissues. He required colloid and inotropic support and peritoneal dialysis for renal failure. He made a full recovery (Fig. 14.7b).

• Meningococcal septicaemia can kill children in hours. Optimal outcome requires immediate recognition, prompt resuscitation and antibiotics.

Figure 14.7 (a) A boy with meningococcal septicaemia receiving intensive care. (b) After full recovery. (Courtesy of Dr Parviz Habibi.)

• Any febrile child with a purpuric rash should be given intramuscular benzylpenicillin immediately and transferred urgently to hospital.

Summary
Pneumococcal infection

- Causes not only minor infections such as otitis media but also invasive disease
- Susceptibility is increased in hyposplenism (e.g. sickle cell disease and nephrotic syndrome)
- Vaccination is included in the standard immunisation schedule.

Table 14-2. Causes of fever and a rash

Maculopapular rash	
Viral	HHV6 or 7 (Roseola infantum) - <2 years old
	Enteroviral rash
	Parvovirus ('slapped cheek') - usually school-age
	Measles - uncommon if immunised
	Rubella - uncommon if immunised
Bacterial	Scarlet fever (group A streptococcus)
	Erythema marginatum - rheumatic fever
	Salmonella typhi (typhoid fever) - classically rose spots
	Lyme disease - erythema migrans
Other	Kawasaki disease
	Juvenile idiopathic arthritis
Vesicular, bullous, pustular	
Viral	Varicella-zoster virus - chickenpox, shingles
	Herpes simplex virus
	Coxsackie - hand, foot and mouth
Bacterial	Impetigo - characteristic crusting
	Boils - infection of hair follicles/sweat glands
	Staphylococcal bullous impetigo
	Staphylococcal scalded skin
	Toxic epidermal necrolysis
Other	Erythema multiforme; Stevens-Johnson syndrome
Petechial, purpuric	
Bacterial	Meningococcal, other bacterial sepsis
	Infective endocarditis
Viral	Enterovirus and other viral infections
Other	Henoch-Schönlein purpura (HSP)
	Thrombocytopenia
	Vasculitis
	Malaria

Summary
Herpes simplex virus infections

- Most are asymptomatic
- Gingivostomatitis - may necessitate intravenous fluids and aciclovir
- Skin manifestations - mucocutaneous junctions, e.g. lips and damaged skin
- Eczema herpeticum - may result in secondary bacterial infection and septicaemia
- Herpetic whitlows - painful pustules on the fingers
- Eye disease - blepharitis, conjunctivitis, corneal ulceration and scarring
- CNS - aseptic meningitis, encephalitis
- Pneumonia and disseminated infection in the immunocompromised.

• Watch for the child with chickenpox whose fever initially settles, but then recurs a few days later - it is likely to be due to secondary bacterial infection.

Clinical features and complications of chickenpox

Exposure
Spread by respiratory droplets
Highly infectious during viral shedding

Illness

Viral shedding

Days: incubation 10–23 (median 14) −2 −1 0 1 2 3 4 5 6 7

Temp (°C): 40°C / 37°C

Papules
Vesicles
Pustules
Crusts

Rash comes in crops for 3–5 days

Complications

Bacterial superinfection
Staphylococcal
Streptococcal
May lead to toxic shock syndrome or necrotising fasciitis

Central nervous system
Cerebellitis
Generalised encephalitis
Aseptic meningitis

Immunocompromised
Haemorrhagic lesions
Pneumonitis
Progressive and disseminated infection
Disseminated intravascular coagulation

Typical vesicular rash
200–500 lesions start on head and trunk, progress to peripheries. (But may be just a few lesions).
Appear as crops of papules, vesicles with surrounding erythema **(Fig. 14.14)** and pustules at different times for up to one week.
Lesions may occur on the palate.
Itchy and scratching may result in permanent, depigmented scar formation or secondary infection.
If new lesions appear beyond 10 days, suggests defective cellular immunity.

- **Beware of admitting a chickenpox contact to a clinical area with immunocompromised children, in whom it can disseminate and be fatal.**
- **Recurrent or multidermatomal shingles suggests a T-cell immune defect.**

Summary
Chickenpox

- Clinical features - fever and itchy, vesicular rash which crops for up to 7 days
- Complications - secondary bacterial infection, encephalitis; disseminated disease in the immunocompromised
- Human varicella zoster immunoglobulin (VZIG) - if immunosuppressed and in contact with chickenpox or if maternal chickenpox shortly before or after delivery
- Treatment is symptomatic; i.v. aciclovir for severe chickenpox or the immunocompromised.

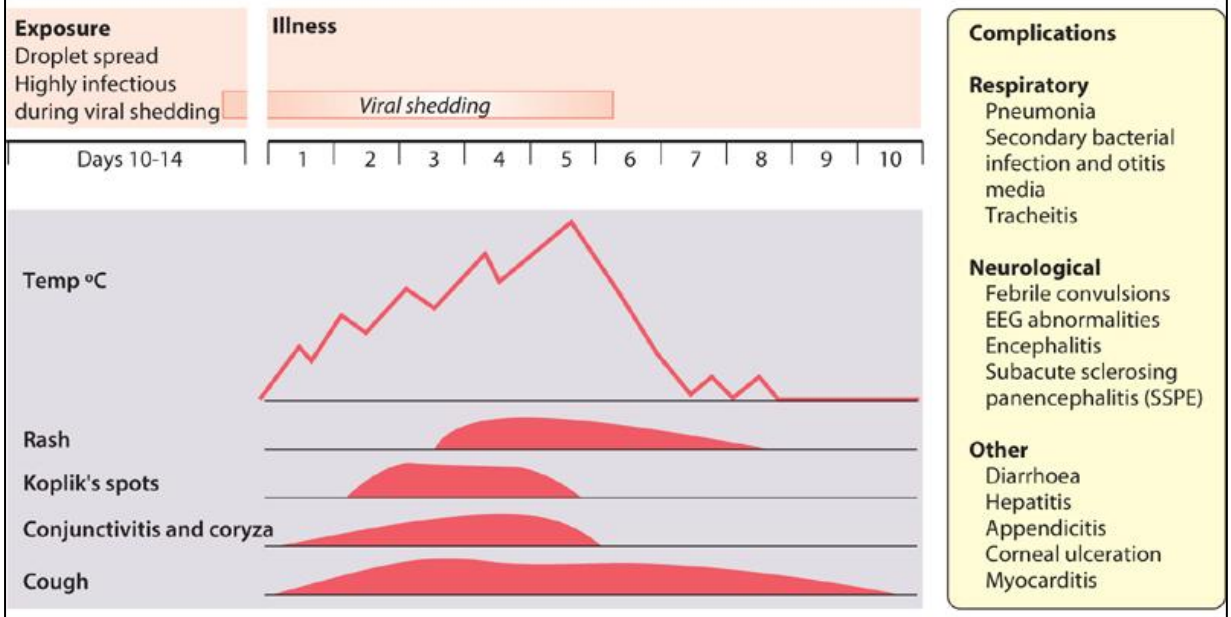
Summary
Parvovirus

- Usually asymptomatic or erythema infectiosum
- Can cause aplastic crisis in haemolytic anaemias (e.g. sickle cell) or the fetus (causes hydrops).

Summary
Enterovirus infection

- Mostly asymptomatic or self-limiting illness with rash, which may be purpuric
- Can cause hand, foot and mouth disease, herpangina, or meningitis/encephalitis.

Clinical features and complications of measles



Koplik's spots
White spots on buccal mucosa, seen against bright red background. Pathognomonic, but difficult to see.

Rash
Spreads downwards, from behind the ears to the whole of the body. Discrete, maculopapular rash initially, becomes blotchy and confluent. May desquamate in the second week.

• Measles remains a major cause of death in childhood in developing countries.

Summary
Measles

- Incidence has declined dramatically since immunisation was introduced; a recent small increase has resulted from the fall in immunisation uptake
- Clinical features: fever, cough, runny nose, conjunctivitis, marked malaise, Koplik spots, maculopapular rash
- Complications: common if malnourished or immunocompromised; major cause of death in developing countries.

Summary
Rubella

- Importance - congenital infection.

Box 14.2 Causes of prolonged fever

Infective:
- Localised infection
- Bacterial infections: e.g. typhoid, *Bartonella henselae* (cat scratch disease), *Brucella*
- Deep abscesses: e.g. intra-abdominal, retro-peritoneal, pelvic
- Infective endocarditis
- Tuberculosis
- Non-tuberculous mycobacterial infections: e.g. *Mycobacterium avium* complex
- Viral infections: e.g. EBV, CMV, HIV
- Parasitic infections: e.g. malaria, toxocariasis

Non-infective:
- Systemic juvenile idiopathic arthritis (SJIA)
- Systemic lupus erythematosus (SLE)
- Vasculitis (including Kawasaki disease)
- Inflammatory bowel disease
- Sarcoidosis
- Malignancy: e.g. leukaemia, lymphoma, neuroblastoma
- Macrophage activation syndromes: e.g. HLH (haemophagocytic lymphohistiocytosis)
- Drug fever
- Fabricated or induced illness.

Summary
Tuberculosis

- TB affects millions of children worldwide; low but increasing incidence in many developed countries
- Clinical features follow a sequence - primary infection, then dormancy, which may be followed by reactivation to post-primary TB
- Diagnosis is often difficult, so decision to treat is usually based on contact history, Mantoux test, interferon-gamma release assays (IGRA), chest X-ray and clinical features. Young children swallow their sputum, so gastric washings are required
- Adherence to drug therapy can be problematic but is essential for successful treatment
- Contact tracing is important
- TB is more difficult to diagnose and more likely to disseminate in the immunosuppressed.

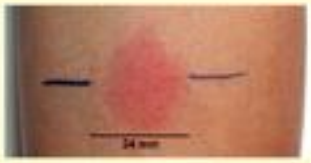
• A febrile child returning from the tropics - commonest causes are non-tropical infections, but consider malaria, typhoid fever and other tropical infections.

Clinical features of TB

Primary infection

Asymptomatic

Nearly half of infants and 90% of older children will show minimal signs and symptoms of infection. A local inflammatory reaction limits the progression of infection. However, the disease remains latent and may therefore develop into active disease at a later time. A Mantoux test may become positive and is sufficient evidence to initiate treatment (Fig. 18.19a).



a) Example of a positive Mantoux test (24 mm induration) A Mantoux test (2 units PPD, PurifiedProtein Derivative) is positive if:
> 10 mm induration (no BCG given)
> 15 mm induration (BCG given)
Implies active infection.

b) Chest X-ray of pulmonary TB. There is marked left hilar lymphadenopathy

Symptomatic

In this case the local host response fails to contain the inhaled tubercle bacilli, allowing spread via the lymphatic system to regional lymph nodes. The lung lesion plus the lymph node constitutes the 'Ghon (or primary) complex'. When the host's cellular immune system responds to the infection (3–6 weeks), mycobacterial replication diminishes but systemic symptoms develop:

- fever
- anorexia and weight loss
- cough
- chest X-ray changes (Fig. 18.19b).

The primary complex usually heals and may calcify. The inflammatory reaction may lead to local enlargement of peribronchial lymph nodes which may cause bronchial obstruction, with collapse and consolidation of the affected lung. Pleural effusions may also be present. Further progression may be halted by the host's immunological response, or there may be local dissemination to other regions of the lung.

Although primary infection most commonly occurs in the lung, it may also involve other organs including gut, skin and superficial lymph nodes. The latter may occasionally caseate forming a 'cold abscess'. Multiple sites may be colonised by metastatic lesions released during the primary infection.

Dormancy and dissemination

Both asymptomatic and symptomatic infections may become dormant but subsequently reactivate and spread by lymphohaematological routes.

Reactivation

Post-primary TB

This may present as local disease or may be widely disseminated, miliary TB to sites such as bones, joints, kidneys, pericardium and CNS. In infants and young children, seeding of the CNS is particularly likely, causing tuberculous meningitis. This was always fatal before antimicrobial therapy was available, and is still associated with significant morbidity and mortality if treatment is not initiated early in the disease.

Immunisation schedule in the UK (2011)

	Birth	1 month	2 months	3 months	4 months	12-13 months	3 years 4 months +	12–13 years	13–18 years
BCG	BCG if at risk								
Hep B	Hep B if at risk	Hep B if at risk	Hep B if at risk			Hep B if at risk			
Diphtheria, tetanus, pertussis, polio, Haemophilus influenzae type B (DTaP/IPV/Hib)			5 in 1	5 in 1	5 in 1				
Pneumococcal vaccine (PCV)			Pneumo vaccine		Pneumo vaccine	Pneumo vaccine			
Meningococcal group C (MenC)				MenC	MenC				
Hib/MenC						Hib/Men C			
MMR						MMR	MMR		
Diphtheria, tetanus, pertussis, polio, (DTaP/IPV)							DTaP/IPV		
Human papilloma-virus (HPV) Girls only								HPV (3 doses)	
Diphtheria tetanus, polio (Td/IPV)									Td/IPV

Box 14.3 Presentation of immune deficiency

- Recurrent (proven) bacterial infections
- Severe infections (e.g. meningitis, osteomyelitis, pneumonia)
- Infections that present atypically, are unusually severe or chronic or fail regular treatment
- Infections caused by an unexpected or opportunistic pathogen or child has been immunised against
- Severe or long-lasting warts, generalised molluscum contagiosum
- Extensive candidiasis
- Complications of vaccination (disseminated BCG)
- Abscesses of internal organs; recurrent subcutaneous abscesses
- Prolonged or recurrent diarrhoea.

Table 14-3. Investigation to identify primary immune deficiency

Immune defect	Investigations
Cellular (T cells)	Full blood count (lymphocyte count) Lymphocyte subsets (to assess CD3+ (total T cell), CD4+ (helper T cell) and CD8+ (cytotoxic T cell) numbers) PHA (phytohaemagglutinin) Ability of T cells to proliferate in response to mitogen
Antibody (humoral; B cells)	Immunoglobulins IgG subclasses (in children >2 years) Specific antibody responses (e.g. tetanus, pneumococcal antibodies) Lymphocyte subsets (B cells present?)
Combined (B and T cells)	Investigations as above Specific genetic/molecular tests for severe combined immunodeficiency (SCID)
Neutrophils	Full blood count (neutropenia) Nitroblue tetrazolium (NBT) - abnormal in chronic granulomatous disease Tests for leucocyte adhesion deficiency - CD11b/CD18 expression Tests of chemotaxis (neutrophil mobility)
Complement/mannose-binding lectin	Tests of classical and alternative complement pathways (CH50, AP50) Assays for individual complement proteins Mannose-binding lectin levels

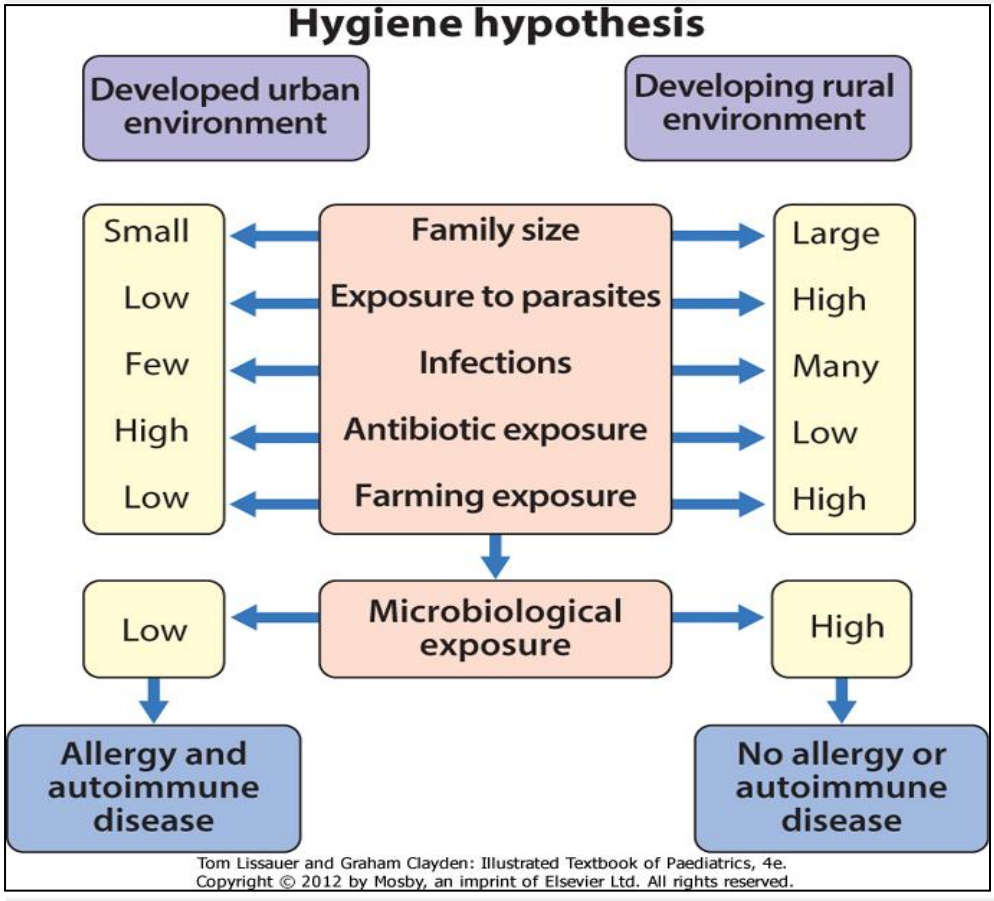
Clinical presentation of primary immune deficiency

Defect	Presentation	Examples
T-cell defects	Severe and/or unusual viral and fungal infections and failure to thrive in first months of life, e.g. severe bronchiolitis, diarrhoea, oral thrush, *Pneumocystis jiroveci (carinii)* pneumonia (PCP).	**Severe combined immunodeficiency (SCID).** Heterogeneous group of inherited disorders of profoundly defective cellular and humoral immunity. Fatal without treatment. **HIV infection** **Wiskott-Aldrich** – triad with thrombocytopenia, and eczema (X-linked). **DiGeorge** – with maldevelopment of the 5th branchial arch causing heart defects, palatal and facial defects, absence of thymus and hypocalcaemia (deletion of section of chromosome 22). **Duncan syndrome (X-linked lymphoproliferative disease)** – inability to make a normal response to Epstein–Barr virus; either succumb to the initial infection or develop secondary lymphoma (X-linked). **Ataxia telangectasia** – defect in DNA repair, also increased risk of lymphoma. Cerebellar ataxia, developmental delay.
B-cell (antibody) defects	In first 2 years (beyond infancy because of passively acquired maternal antibody) – severe bacterial infections, especially ear, sinus, pulmonary and skin infections; recurrent diarrhoea and failure to thrive. Recurrent pneumonias can lead to bronchiectasis; recurrent ear infections to impaired hearing.	**X-linked (Bruton) agammaglobulinaemia.** Abnormal tyrosine kinase gene; essential for B-cell maturation. **Common variable immune deficiency (CVID) –** B-cell deficiency. High risk of autoimmune disorders and malignancy. Later onset than Bruton agammaglobulinaemia. **Hyper IgM syndrome** – B cells produce IgM but prevented from switching to IgG and IgA. **Selective IgA deficiency** – most common primary immune defect. Usually asymptomatic, or recurrent ear, sinus and pulmonary infections.
Neutrophil defects	Recurrent bacterial infections – abscesses (skin, lymph nodes, lung, liver, spleen, bone), poor wound healing, perianal disease and periodontal infections; invasive fungal infections, such as aspergillosis. Diarrhoea and failure to thrive. Granulomas from chronic inflammation.	**Chronic granulomatous disease** – most are X-linked recessive, some autosomal recessive. Defect in phagocytosis as fail to produce superoxide after ingestion of micro-organisms.
Leucocyte function defects	Delayed separation of umbilical cord, delayed wound healing, chronic skin ulcers and deep-seated infections.	**Leucocyte adhesion deficiency (LAD)** – deficiency of neutrophil surface adhesion molecules, CD18, CD11b, leads to inability of neutrophils to migrate to sites of infection/inflammation.
Complement defects	Recurrent bacterial infections. SLE-like illness. Recurrent meningococcal infections – with deficiency of the terminal complement components (C5b to C9).	**Early complement component deficiency** **Terminal complement component deficiency** **Mannose-binding lectin (MBL) deficiency.**

Chapter 15: Allergy

Box 15.1 Allergy definitions

- *Hypersensitivity* - objectively reproducible symptoms or signs following exposure to a defined stimulus (e.g. food, drug, pollen) at a dose which is tolerated by normal people.
- *Allergy* - a hypersensitivity reaction initiated by specific immunological mechanisms. This can be IgE mediated (e.g. peanut allergy) or non-IgE mediated (e.g. coeliac disease).
- *Atopy* - a personal and/or familial tendency to produce IgE antibodies in response to ordinary exposures to potential allergens, usually proteins. Strongly associated with asthma, allergic rhinitis and conjunctivitis, eczema and food allergy.
- *Anaphylaxis* - a serious allergic reaction that is rapid in onset and may cause death.



Summary
Paediatric allergy

- Includes food allergy, eczema, allergic rhinitis and conjunctivitis, asthma, urticaria, insect sting hypersensitivity and anaphylaxis
- Occurs when a genetically susceptible person reacts abnormally to an environmental antigen
- There is an 'allergic march' of disorders
- Different allergic diseases often coexist - if a child has one, look for others.

Examples of food allergy and hypersensitivity to milk

Condition	Clinical manifestation
IgE-mediated food allergy • Immediate cow's milk allergy	This 6-month-old breast-fed infant developed an allergic reaction **(a)**, with widespread urticaria immediately after the first formula feed. Skin-prick test were strongly positive to cow's milk. Widespread urticaria and lip swelling after milk ingestion are shown in **(b)** and **(c)** **(a) Clinical features of an acute allergic reaction:** **Mild reaction** • Urticaria and itchy skin • Facial swelling **Severe reaction** • Wheeze • Stridor • Abdominal pain, vomiting, diarrhoea • Shock, collapse
	 
Non-IgE-mediated cow's milk allergy	A 4-month-old infant, formula fed since birth, has loose stools and is failing to thrive. Skin prick test to cow's milk is negative. Elimination of cow's milk results in resolution of symptoms which return on trial re-introduction.
Non-allergic food hypersensitivity • Temporary lactose intolerance	Previously well 12-month-old infant develops diarrhoea and vomiting. The vomiting settles but watery stools continue for several weeks. Stool sample – no pathogens but positive for reducing substances. Diagnosis – temporary lactose intolerance.

Summary
Food allergy

- Affects up to 6% of children
- The most common causes are milk, egg, nuts, seafood, wheat, legumes, seeds and fruits
- Diagnosis of IgE-mediated food allergy is based on a suggestive history supported by skin-prick tests or specific IgE antibodies in blood
- Supervised food challenge is sometimes necessary to clarify the diagnosis
- Those at risk of a severe reaction, e.g. with coexistent asthma, should carry an epinephrine (adrenaline) auto-injector.

Box 15.2 Range of treatment for allergic rhinoconjunctivitis

- Second-generation non-sedating antihistamines (used topically or systemically)
- Topical corticosteroid nasal or eye preparations (the latter under specialist ophthalmology supervision)
- Cromoglycate eye drops
- Leukotriene receptor antagonists, e.g. montelukast
- Nasal decongestants (use for no more than 7-10 days due to risk of rebound effect)
- Allergen immunotherapy - sublingual or subcutaneous (limited by anaphylaxis risk)
- Systemic corticosteroids should not be used due to the risk of adverse effects.

Box 15.3 Classification of urticaria/angioedema

- Acute - resolve within 6 weeks; allergy such as food or drug reactions, or infection are common triggers
- Chronic idiopathic - intermittent for at least 6 weeks
- Physical urticarias
  - - Cold, delayed pressure, heat contact, solar, vibratory urticaria
- Other causes
  - - Water (aquagenic), sweating (cholinergic), exercise-induced
  - - Aspirin and other non-steroidal anti-inflammatory agents
  - - C1-esterase inhibitor deficiency (angioedema, but no urticaria or pruritus).

Summary
Insect sting hypersensitivity

- Mainly to bee and wasp stings
- Following a severe reaction, an epinephrine (adrenaline) auto-injector should be carried
- Immunotherapy is highly effective in children who have had a severe reaction.

Chapter 16: Respiratory disorders

Summary
Acute otitis media

- Can only be diagnosed by examining the tympanic membrane
- Antibiotics marginally shorten the duration of pain but do not reduce hearing loss
- If recurrent, may result in otitis media with effusion, which may cause speech and learning difficulties from hearing loss.

Box 16.1 Differential diagnosis of acute upper airways obstruction

Common causes

- Viral laryngotracheobronchitis ('croup' - very common)

Rare causes

- Epiglottitis
- Bacterial tracheitis
- Inhalation of smoke and hot air in fires
- Trauma to the throat
- Retropharyngeal abscess
- Laryngeal foreign body
- Allergic laryngeal angioedema (seen in anaphylaxis and recurrent croup)
- Hypocalcaemia due to poor vitamin D intake
- Infectious mononucleosis causing severe lymph node swelling
- Measles
- Diphtheria

• Basic management of acute upper airways obstruction

- **Do not examine the throat!**
- **Reduce anxiety by being calm, confident and well organised.**
- **Observe carefully for signs of hypoxia or deterioration.**
- **If severe, administer nebulised epinephrine (adrenaline) and contact an anaesthetist.**
- **If respiratory failure develops from increasing airways obstruction, exhaustion or secretions blocking the airway, urgent tracheal intubation is required.**

Table 16-1. Clinical features of croup (viral laryngotracheitis) and epiglottitis

	Croup	Epiglottitis
Onset	Over days	Over hours
Preceding coryza	Yes	No
Cough	Severe, barking	Absent or slight
Able to drink	Yes	No
Drooling saliva	No	Yes
Appearance	Unwell	Toxic, very ill
Fever	<38.5°C	>38.5°C
Stridor	Harsh, rasping	Soft, whispering
Voice, cry	Hoarse	Muffled, reluctant to speak

Summary
Pertussis

- Caused by *Bordetella pertussis*
- Paroxysmal cough followed by inspiratory whoop and vomiting; in infants, apnoea rather than whoop, which is potentially dangerous
- Diagnosis: culture of organism on per-nasal swab, marked lymphocytosis on blood film.

Case History 16.1 Acute epiglottitis
This 5-year-old girl developed a severe sore throat, drooling of saliva, a high fever and increasing difficulty breathing over 8 h (Fig. 16.4a) Epiglottitis was diagnosed and her airway was guaranteed with a nasotracheal tube. Antibiotics were started immediately (Fig. 16.4b,c). She made a full recovery.

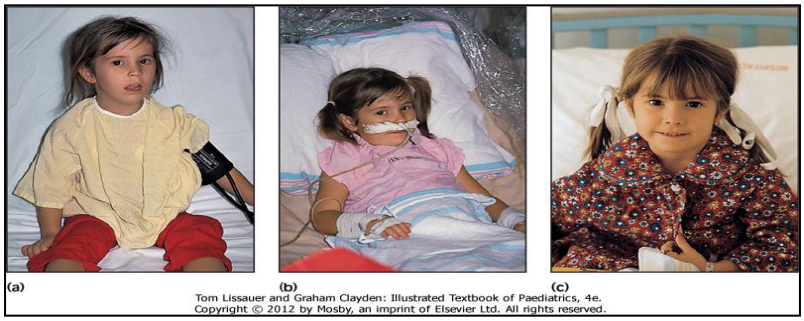
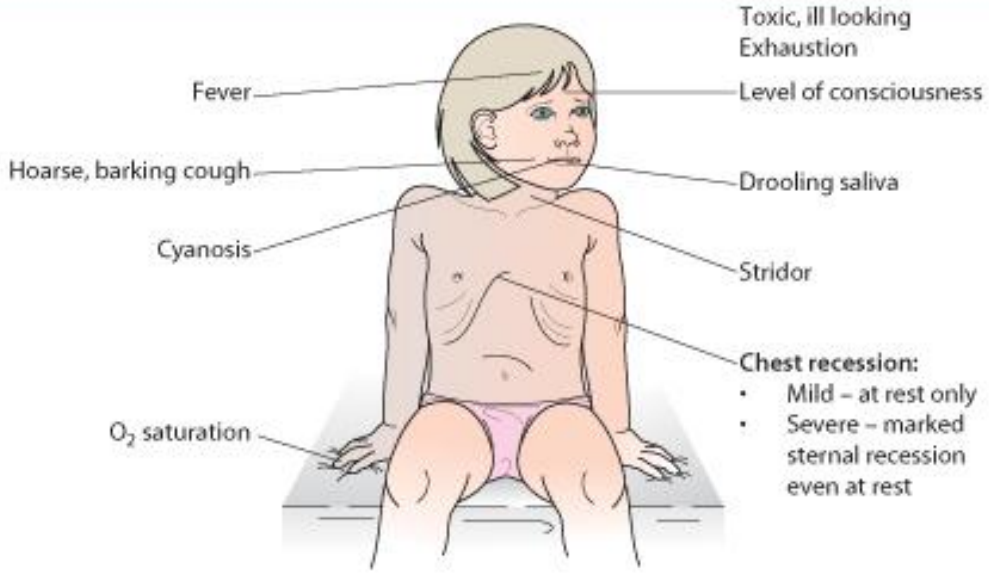


Figure 16.4 Acute epiglottitis. (a) At presentation. (b) At 16 h, with nasotracheal and nasogastric tubes and an indwelling cannula for intravenous antibiotics. (c) At 36 h, following removal of the nasotracheal and nasogastric tubes.

Clinical features to assess



Clinical conditions

Croup
- Mostly viral
- 6 months to 6 years of age
- Harsh, loud stridor
- Coryza and mild fever, hoarse voice

Epiglottitis:
- Caused by *H. influenzae* type b, rare since Hib immunisation
- Mostly aged 1–6 years
- Acute, life-threatening illness
- High fever, ill, toxic-looking
- Painful throat, unable to swallow saliva, which drools down the chin

Bacterial tracheitis:
- High fever, toxic
- Loud, harsh stridor

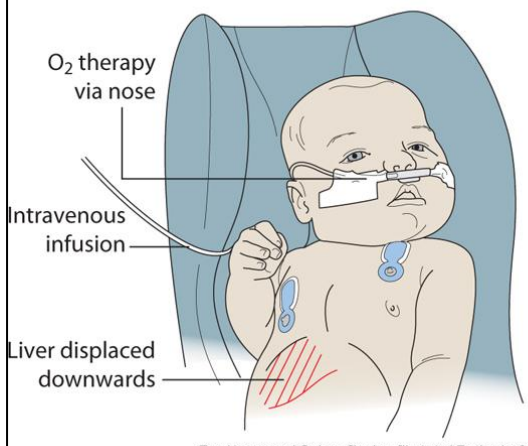
Inhaled foreign body
- Choking on peanut or toy in mouth
- Sudden onset of cough or respiratory distress

Laryngomalacia or congenital airway abnormality:
- Recurrent or continuous stridor since birth

Other rare causes:
- See Box 16.1

Child with stridor

Bronchiolitis



Apnoea in infants <4 months

Sharp, dry cough

Cyanosis or pallor

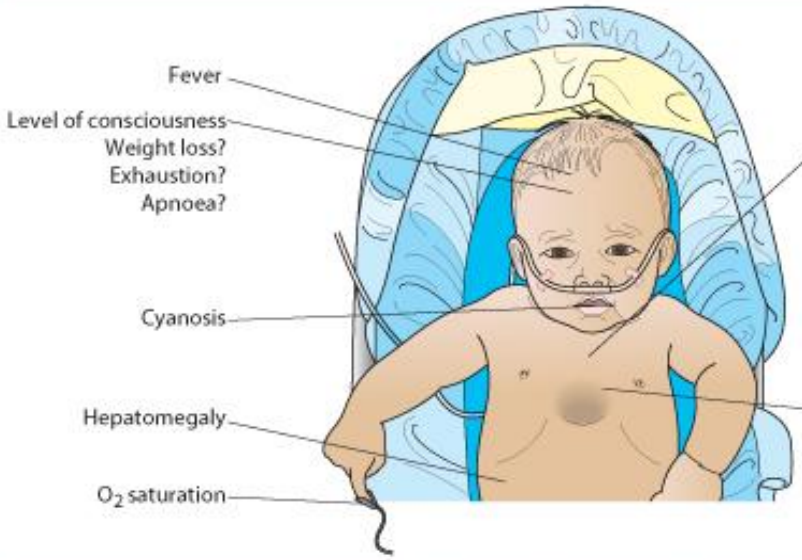
Hyperinflation of the chest:
- sternum prominent
- liver displaced downwards

Subcostal and intercostal recession

Auscultation:
- fine end-inspiratory crackles
- prolonged expiration

The infant with tachypnoea or wheeze

Clinical features to assess



Breathing:
Too breathless to feed?
Respiratory rate –
> 40 breaths/min
Chest hyperexpansion
Chest recession
Use of accessory muscles
Expiratory grunting, nasal flaring
Auscultation, percussion – abnormal signs

Heart:
Heart rate –
> 160 beats/min
Heart murmur

Clinical conditions to consider

Bronchiolitis
- Age 1–9 months
- Poor feeding, apnoea, dry cough
- Laboured breathing – chest recession, hyperinflation of the chest, fine end-inspiratory crackles, wheeze, liver displaced downwards
- Apnoea, cyanosis, respiratory failure
- Increased severity with bronchopulmonary dysplasia in preterm or congenital heart disease

Pneumonia
- Fever, poor feeding, cough, lethargy, cyanosis
- Tachypnoea, nasal flaring, chest recession, wheeze and end-inspiratory coarse crackles over the affected area
- O_2 saturation may be decreased
- Chest X-ray – consolidation, parapneumonic effusion or empyema

Transient early wheezing – with viral infections, risk increased in preterm and maternal smoking

Non-atopic wheezing – following viral lower respiratory infection

Atopic asthma – recurrent wheezing, eczema, positive family history of allergy/atopy

Cardiac failure – respiratory distress, heart murmur, hepatomegaly

Inhaled foreign body – choking on peanut or toy, etc.
Aspiration of feeds – especially with neuromuscular disorder
Other causes – see Box 16.2

Box 16.2 Causes of childhood wheeze

- Transient early wheezing
- Atopic asthma (IgE-mediated)
- Non-atopic asthma
- Recurrent aspiration of feeds
- Inhaled foreign body
- Cystic fibrosis
- Recurrent anaphylaxis in a child with food allergies
- Congenital abnormality of lung, airway or heart
- Idiopathic.

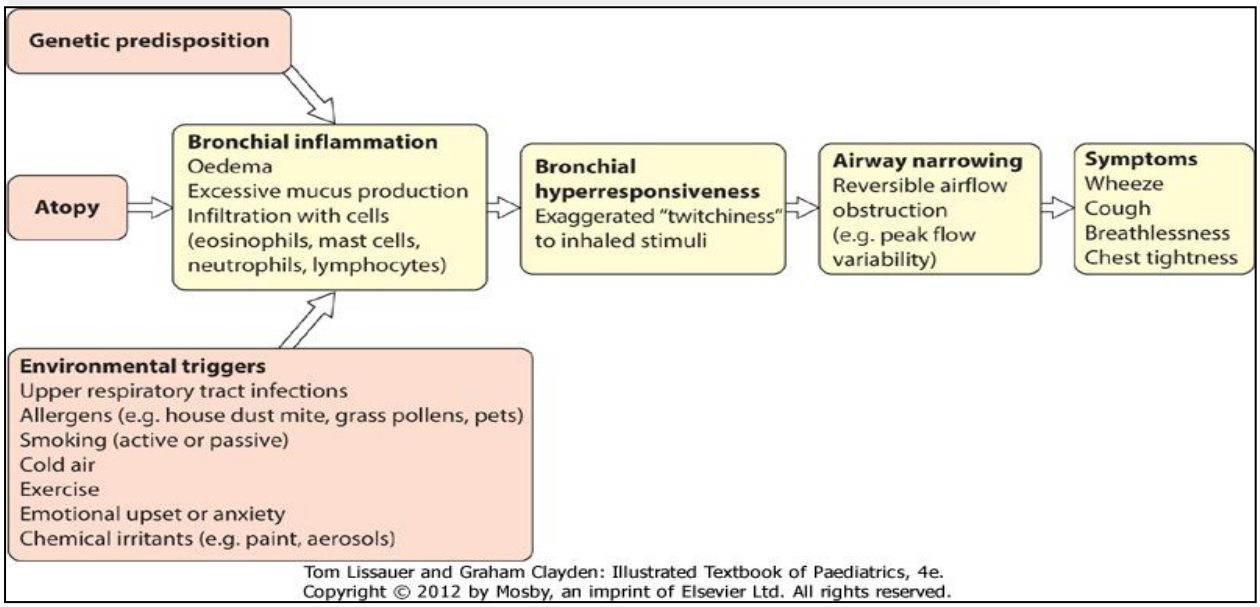


Figure 16.10 Pathophysiology of asthma.

Assessment of the child with chronic asthma

Clinical features to check

Growth and nutrition

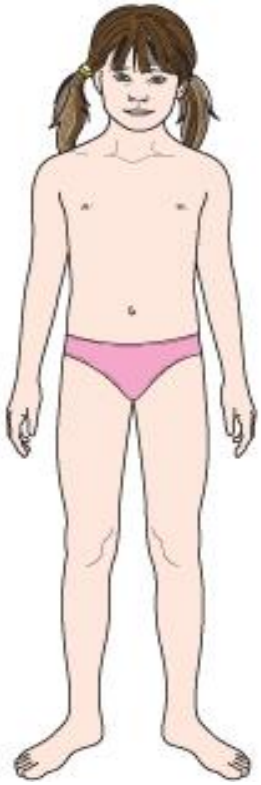
Peak flow/spirometry

Chest for:
Hyperinflation
Harrison's sulcus
Wheeze

Are there other allergic disorders?
- Allergic rhinitis
- Eczema, etc.

If there is:
- Sputum
- Finger clubbing
- Growth failure

– If present, other causes should be sought



Monitor:
- Peak flow diary
- Severity and frequency of symptoms
- Exercise tolerance
- Interference with life, time off school
- Is sleep disturbed?
- Use of preventer and reliever medication – are they appropriate?
- Inhaler technique

Consider triggers:
- Allergic rhinitis needing treatment?
- Allergens - animal dander, etc.
- Stress

Choosing the correct inhaler

Inhaled drugs may be administered via a variety of devices, chosen according to the child's age and preference:

- *Pressurised metered dose inhaler (pMDI) and spacer* (Fig. 16.13).
    - \- Appropriate for all age groups: 0-2 years, spacer and facemask; >2 years, spacer alone
    - \- A spacer is recommended for all children as it increases drug deposition to the lungs
    - \- Useful for acute asthma attacks when poor inspiratory effort may impair the use of inhalers direct to the mouth
- *Breath-actuated metered dose inhalers* (e.g. *Autohaler*, *Easibreath*): 6+ years. Less coordination needed than a pMDI without spacer. Useful for delivering β-agonists when 'out and about' in older children
- *Dry powder inhaler*: 4+ years (Fig. 16.14). Needs a good inspiratory flow, therefore less good in severe asthma and during an asthma attack. Also easy to use when 'out and about' in older children
- *Nebuliser*: any age (Fig. 16.15). Only used in acute asthma where oxygen is needed in addition to inhaled drugs; occasionally used at home as part of an acute management plan in those with rapid-onset severe asthma (brittle asthma).

Many children fail to gain the benefit of their treatment because they cannot use the inhaler correctly. This must be demonstrated and the child's ability to use it checked. In young children, parents need to be skilled in assisting their child to use the inhaler correctly. Assessing and reassessing inhaler technique is vital to good management and should be a routine part of any review.

A stepwise approach to the treatment of chronic asthma

Step 5: Continuous frequent use of oral steroids
Daily oral steroids in the lowest dose for adequate control
Refer for specialist care – may require immunosuppressant or immunomodulation therapy and psychological input

Step 4: Persistent poor control
5 years or over:
- Increase inhaled steroids to maximum recommended dose
- If not responding, go to step 5 and refer to respiratory paediatrician

< 5 years:
refer to respiratory paediatrician

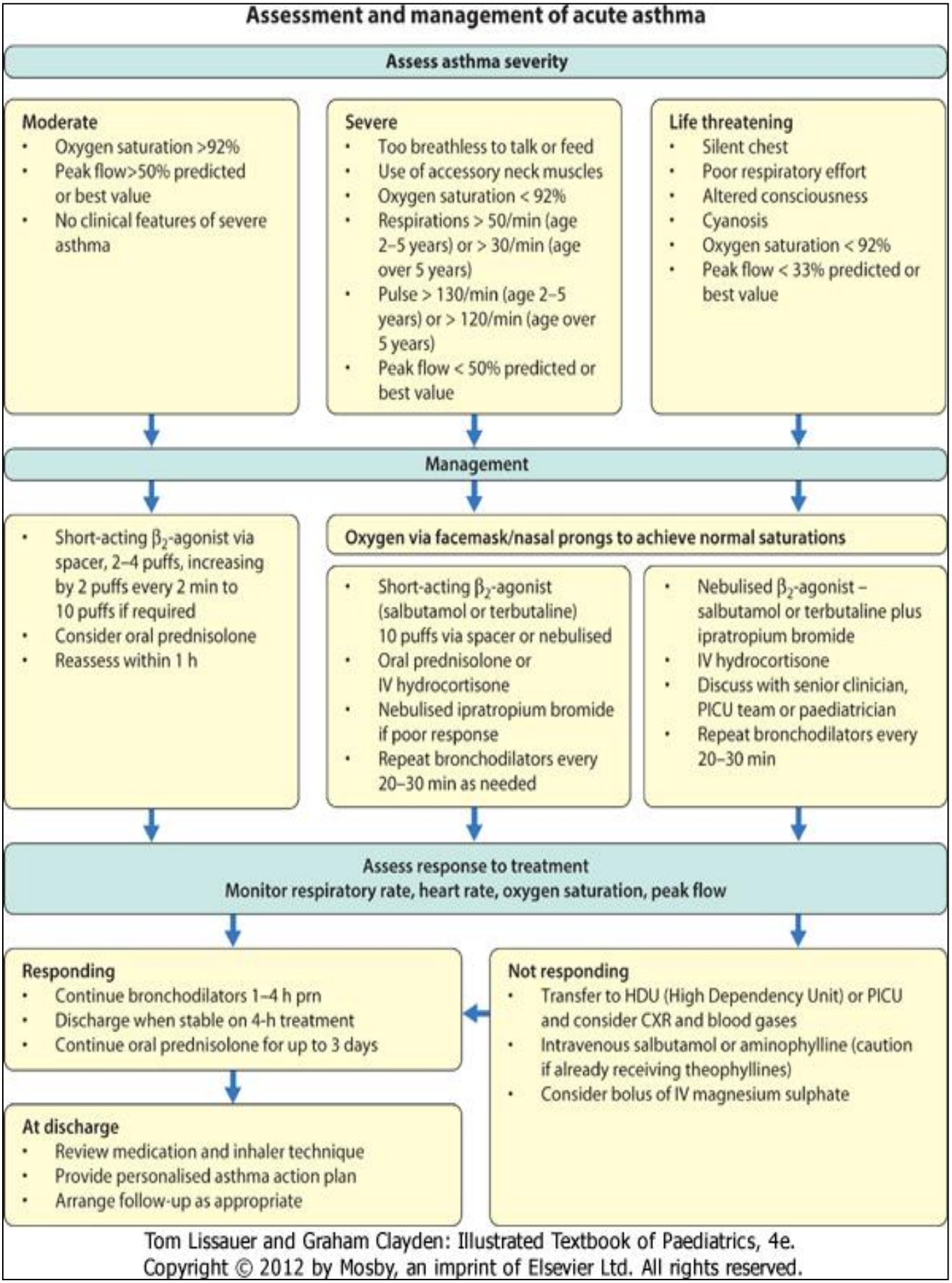
Step 3: Poorly controlled on conventional doses of inhaled steroids – 'add-on' therapy
5 years or over:
i) Add inhaled long-acting β_2-agonist (LABA)
ii) Assess control of asthma:
- good response to LABA – continue
- benefit from LABA but control inadequate – go to step 4
- no response to LABA – stop LABA and try leukotriene receptor antagonist or theophyllines

< 5 years:
i) consider adding in leukotriene receptor agonists to inhaled steroids
ii) In children <2 years, consider referral to respiratory paediatrician

Step 2: Regular preventer therapy – requires 3 or more β_2-agonist inhalations per week
Add inhaled steroid
Start at dose appropriate to severity of disease
< 5 years:
consider oral leukotriene receptor antagonist if inhalers not tolerated

Step 1: Mild intermittent asthma
Inhaled short-acting β_2-agonist as required
Infants and young children – consider inhaled ipratropium bromide

There is a logical stepwise progression to treatment. This is determined by the frequency and severity of symptoms and the response to treatment. The aim is to gain control of symptoms and to then step down treatment over the next few months.



Assessment of the child with acute asthma

Determine the severity of the attack
(see Fig 16.16)
- Mild
- Moderate
- Severe
- Life-threatening

Too breathless to talk or eat?

Increased work of breathing
- Tachypnoea – severe if >30 breaths/min

Chest recession:
- Moderate – some intercostal recession
- Severe – use of accessory neck muscles
- Life-threatening – poor respiratory effort

Auscultation:
- Wheeze
- Silent chest – poor air entry in life-threatening

Pulse:
- Severe – >120 beats/min

Level of consciousness – altered in life-threatening
Exhaustion

Tongue:
- Cyanosis in life-threatening

Peak flow (% predicted):
- Moderate >50%
- Severe <50%
- Life-threatening <33%

O_2 saturation:
- Moderate >92%
- Severe or life-threatening <92%

Is there a trigger for the attack?:
- URTI or other viral illness
- Pneumonia
- Allergen, e.g. animal dander
- Exercise
- Cold air

Box 16.3 Causes of recurrent or persistent cough

- Recurrent respiratory infections
- Post-specific respiratory infections (e.g. pertussis, RSV, *Mycoplasma*)
- Asthma
- Suppurative lung diseases (e.g. cystic fibrosis, ciliary dyskinesia or immune deficiency)
- Recurrent aspiration (± gastro-oesophageal reflux)
- Persistent endobronchial infection
- Inhaled foreign body
- Cigarette smoking (active or passive)
- Tuberculosis
- Habit cough
- Airway anomalies (e.g. tracheo-bronchomalacia, tracheo-oesophageal fistula).

Chapter 17: Cardiac disorders

Box 17.1 The most common congenital heart lesions

Left-to-right shunts (breathless)
- Ventricular septal defect 30%
- Persistent arterial duct 12%
- Atrial septal defect 7%

Right-to-left shunts (blue)
- Tetralogy of Fallot 5%
- Transposition of the great arteries 5%

Common mixing (breathless and blue)
- Atrioventricular septal defect (complete) 2%

Outflow obstruction in a well child (asymptomatic with a murmur)
- Pulmonary stenosis 7%
- Aortic stenosis 5%

Outflow obstruction in a sick neonate (collapsed with shock)
- Coarctation of the aorta 5%.

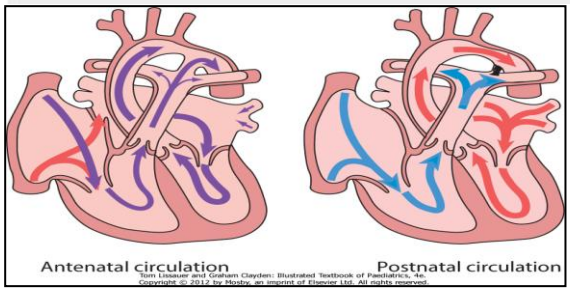


Figure 17.1 Changes in the circulation from the fetus to the newborn. When congenital heart lesions rely on blood flow through the duct (a duct-dependent circulation), there will be a dramatic deterioration in the clinical condition when the duct closes.

Table 17-1. Causes of congenital heart disease

	Cardiac abnormalities	Frequency
Maternal disorders		
Rubella infection	Peripheral pulmonary stenosis, PDA	30-35%
Systemic lupus erythematosus (SLE)	Complete heart block (anti-Ro and anti-La antibody)	35%
Diabetes mellitus	Incidence increased overall	2%
Maternal drugs		
Warfarin therapy	Pulmonary valve stenosis, PDA	5%
Fetal alcohol syndrome	ASD, VSD, tetralogy of Fallot	25%
Chromosomal abnormality		
Down syndrome (trisomy 21)	Atrioventricular septal defect, VSD	30%
Edwards syndrome (trisomy 18)	Complex	60-80%
Patau syndrome (trisomy 13)	Complex	70%
Turner syndrome (45XO)	Aortic valve stenosis, coarctation of the aorta	15%
Chromosome 22q11.2 deletion	Aortic arch anomalies, tetralogy of Fallot, common arterial trunk	80%
Williams syndrome (7q11.23 microdeletion)	Supravalvular aortic stenosis, peripheral pulmonary artery stenosis	85%
Noonan syndrome (PTPN11 mutation and others)	Hypertrophic cardiomyopathy, atrial septal defect, pulmonary valve stenosis	50%

ASD, atrial septal defect; PDA, persistent ductus arteriosus; VSD, ventricular septal defect.

Box 17.2 Causes of heart failure

1. Neonates - obstructed (duct-dependent) systemic circulation

- Hypoplastic left heart syndrome
- Critical aortic valve stenosis
- Severe coarctation of the aorta
- Interruption of the aortic arch

2. Infants (high pulmonary blood flow)

- Ventricular septal defect
- Atrioventricular septal defect
- Large persistent ductus arteriosus

3. Older children and adolescents (right or left heart failure)

- Eisenmenger syndrome (right heart failure only)
- Rheumatic heart disease
- Cardiomyopathy.

Table 17-2. Types of presentation with congenital heart disease

Type of lesion	Left-to-right shunt	Right-to-left shunt	Common mixing	Well children with obstruction	Sick neonates with obstruction
Symptoms	Breathless or asymptomatic	Blue	Breathless and blue	Asymptomatic	Collapsed with shock
Examples	ASD	Tetralogy of Fallot	AVSD	AS	Coarctation
	VSD PDA	TGA	Complex congenital heart disease	PS Adult-type CoA	HLHS

ASD, atrial septal defect; VSD, ventricular septal defect; PDA, patent ductus arteriosus; TGA, transposition of the great arteries; AVSD, atrioventricular; AS, aortic stenosis; PS, pulmonary stenosis; CoA, coarctation of the aorta; HLHS, hypoplastic left heart syndrome.

Case History 17.1 Shock

A 2-day-old baby had been discharged home the day after delivery following a normal routine examination. He suddenly collapsed and was rushed to hospital. He was pale, with grey lips. The right brachial pulse could just be felt, the femoral pulses were impalpable and his liver was significantly enlarged. Blood gases showed a severe metabolic acidosis. The differential diagnosis was:

- Congenital heart disease
- Septicaemia
- Inherited disorder of metabolism.

He was ventilated and treated with volume support. Blood cultures were taken and antibiotics started for possible sepsis. Blood and urine samples were taken for an amino acid screen and urine for organic acids. As the femoral pulses remained impalpable, a prostaglandin infusion was started. Within 2 hours, he was pink and well perfused and the acidosis was resolving. Severe coarctation of the aorta (Fig. 17.3) was diagnosed on echocardiography. He had developed shock from a left heart outflow tract obstruction once the arterial duct had closed.

• Maintaining ductal patency is the key to early survival in neonates with a duct-dependent circulation.

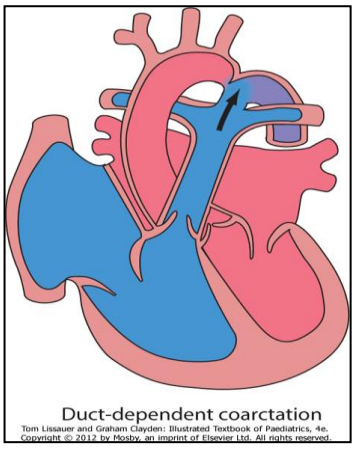


Figure 17.3 The systemic circulation is maintained by blood flowing right to left across the ductus arteriosus - a duct-dependent systemic circulation.

Case History 17.2 Heart failure

A 5-week-old female infant was referred to hospital because of wheezing, poor feeding and poor weight gain during the previous 2 weeks. Before this, she had been well. Her routine neonatal examination had been normal. She was tachypnoeic (50-60 breaths/min) and there was some sternal and intercostal recession. The pulses were normal. There was a thrill, a pansystolic murmur at the lower left sternal edge and a slightly accentuated pulmonary component to the second heart sound. There were scattered wheezes. The liver was enlarged, palpable at two fingerbreadths below the costal margin. The ECG was unremarkable. The chest radiograph showed cardiomegaly and increased pulmonary vascular markings. An echocardiogram showed a moderate-sized ventricular septal defect (VSD) (Fig. 17.4). Treatment was medical with diuretics and captopril. The VSD closed spontaneously at 18 months.

This infant developed heart failure from a moderate VSD presenting at several weeks of age when the pulmonary resistance fell, causing increased left-to-right shunting of blood. The defect closed spontaneously.

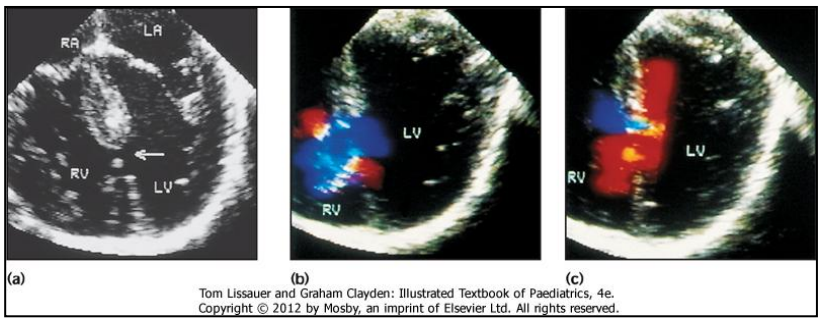


Figure 17.4 (a) Echocardiogram showing a medium-sized muscular ventricular septal defect (arrow). (b) The colour Doppler shows a left-to-right shunt (blue) during systole. (c) There is also a small right-to-left shunt (red) during diastole (RA, right atrium; LA, left atrium; RV, right ventricle; LV, left ventricle).

Summary

Presentation of congenital heart disease

- Antenatal ultrasound screening - increasing proportion detected
- Detection of a heart murmur - need to differentiate innocent from pathological murmur
- Cyanosis - if duct dependent, prostaglandin to maintain ductal patency is vital for initial survival
- Heart failure - usually from left-to-right shunt when pulmonary vascular resistance falls
- Shock - when duct closes in severe left heart obstruction.

Box 17.3 ECGs in children

Important features

- Arrhythmias
- Superior QRS axis (negative deflection in AVF) (see Fig. 17.5f)
- Right ventricular hypertrophy (upright T wave in V_1, over 1 month of age) (see Fig. 17.6e)
- Left ventricular strain (inverted T wave in V_6) (see Fig. 17.13d)

Pitfalls

- P-wave morphology is rarely helpful in children
- Partial right bundle branch block - most are normal children, although it is common in ASD
- Sinus arrhythmia is a normal finding.

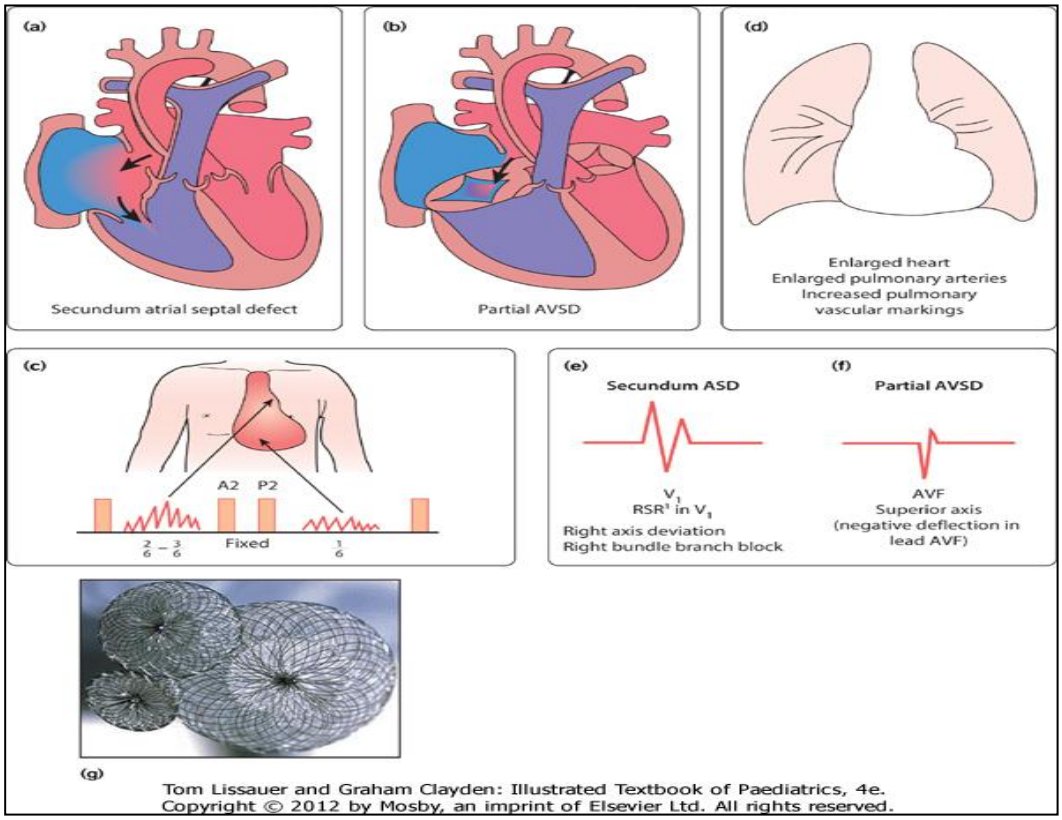


Figure 17.5 Atrial septal defect (a)The ostium secundum atrial septal defect (ASD) is a deficiency of the foramen ovale and surrounding atrial septum. (b) Partial atrioventricular septal defect (AVSD) is a deficiency of the atrioventricular septum. (c) Murmur. (d) Chest radiograph. (e,f) ECG. (g) Examples of an occlusion device used to close secundum atrial septal defects.

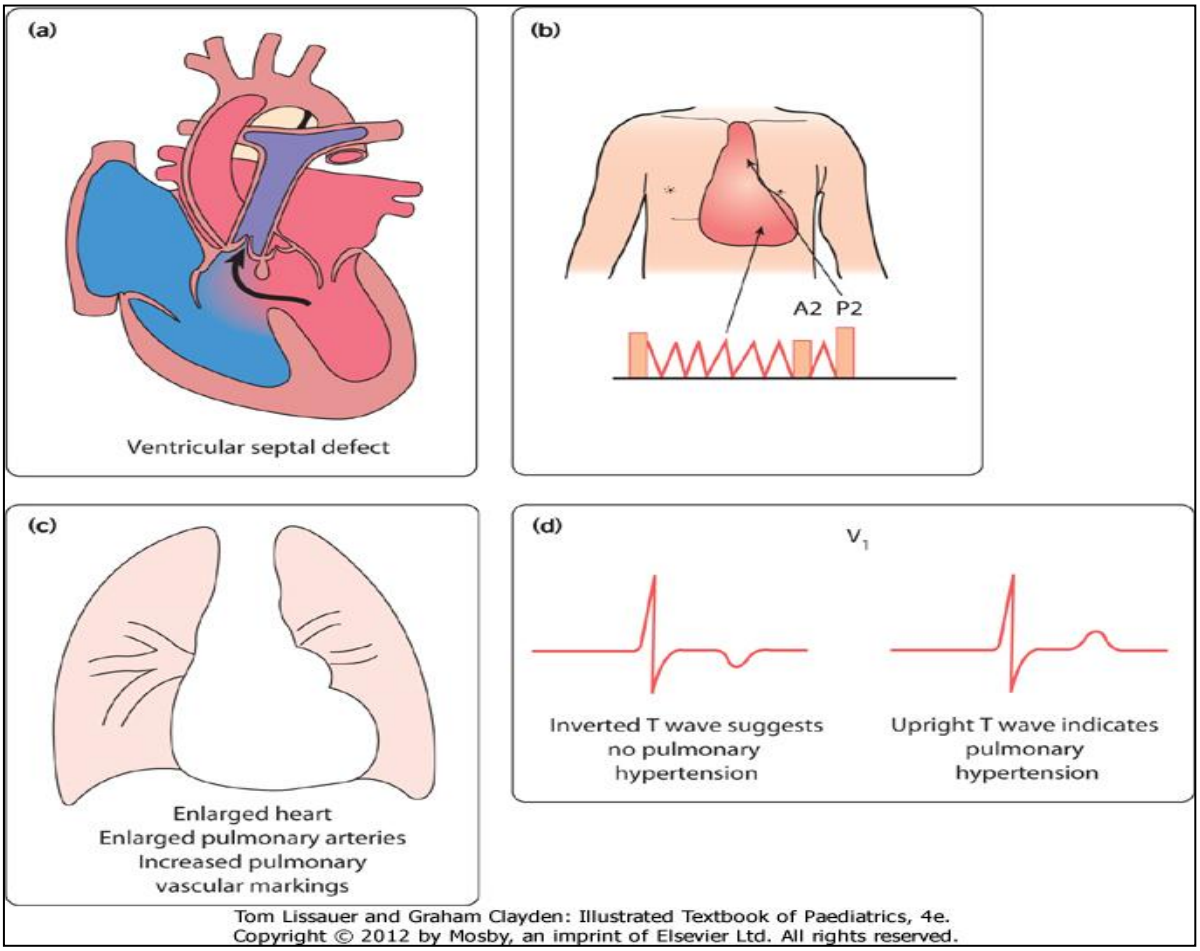


Figure 17.6 Ventricular septal defect. (a) Ventricular septal defect showing a left-to-right shunt. (b) Murmur. (c) Chest radiograph. (d) ECG.

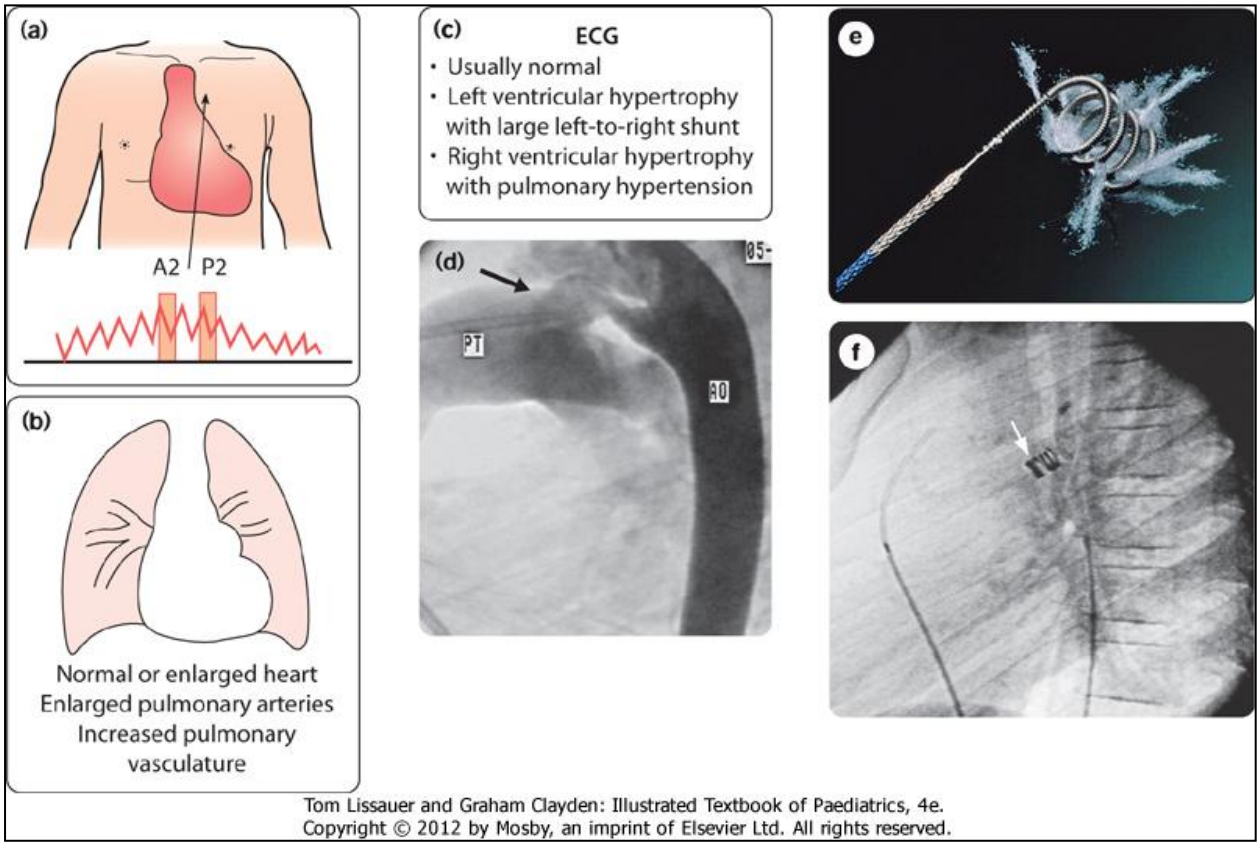


Figure 17.7 Persistent ductus arteriosus. (a) Murmur. (b) Chest radiograph. (c) ECG. (d) A persistent ductus arteriosus visualised on angiography. (e) A coil used to close ducts. It is passed through a catheter via the femoral artery or vein. (f) Angiogram to show coil in the duct. (PT, pulmonary trunk; AO, aorta.)

Summary
Left-to-right shunts

Lesion	Symptoms	Signs	Management
ASD			
Secundum	None	ESM at ULSE Fixed split S_2	Catheter device closure at 3-5 years
Partial AVSD	None	ESM at ULSE	Surgery at 3 years
		Fixed split S_2	
		Pansystolic murmur at apex	
VSD			
Small (80-90% of cases)	None	Pansystolic murmur at LLSE	None
Large (10-20% if cases)	Heart failure	Active precordium, loud P_2, soft murmur, tachypnoea, hepatomegaly	Diuretics, captopril, calories Surgery at 3-6 months old
PDA	None	Continuous murmur at ULSE ± bounding pulses	Coil or device closure at cardiac catheter at 1 year, or ligation

ASD, atrial septal defect; AVSD, atrioventricular septal defect; VSD, ventricular septal defect; PDA, persistent ductus arteriosus; ESM, ejection systolic murmur; ULSE, upper left sternal edge; LLSE, lower left sternal edge.

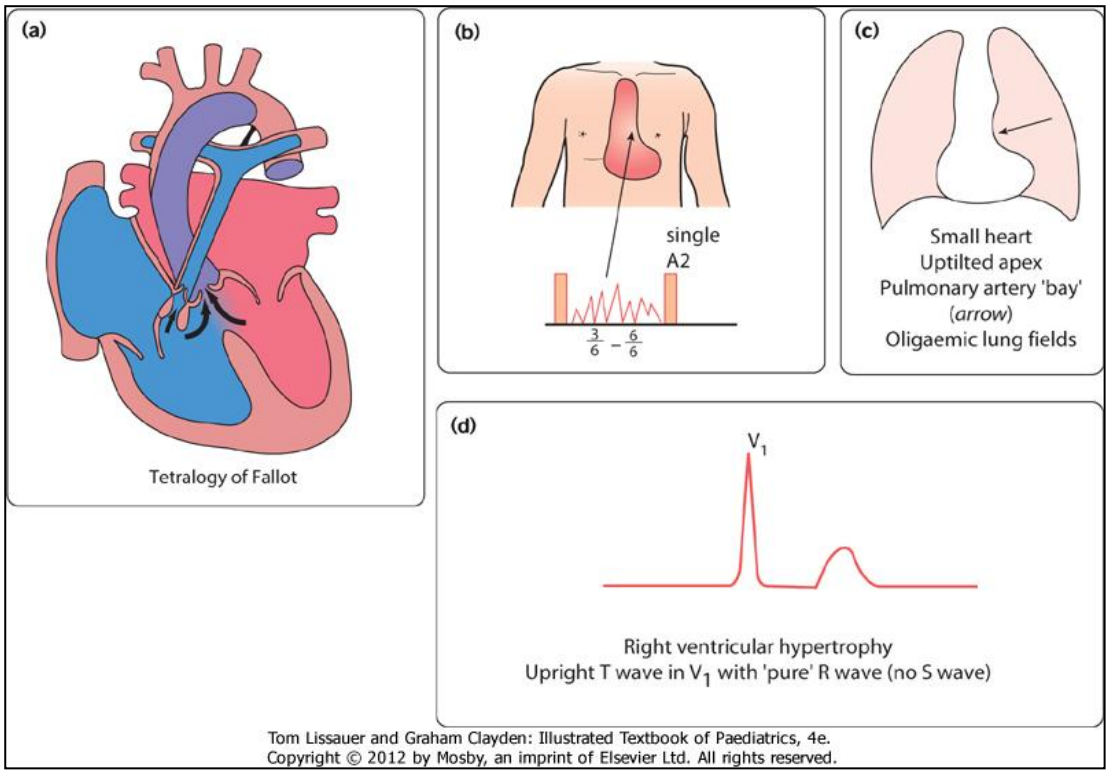


Figure 17.8 Tetralogy of Fallot. (a) Tetralogy of Fallot. The right ventricular outflow tract obstruction results in blood flowing from right to left across the ventricular septal defect (b) Murmur. (c) Chest radiograph. (d) ECG.

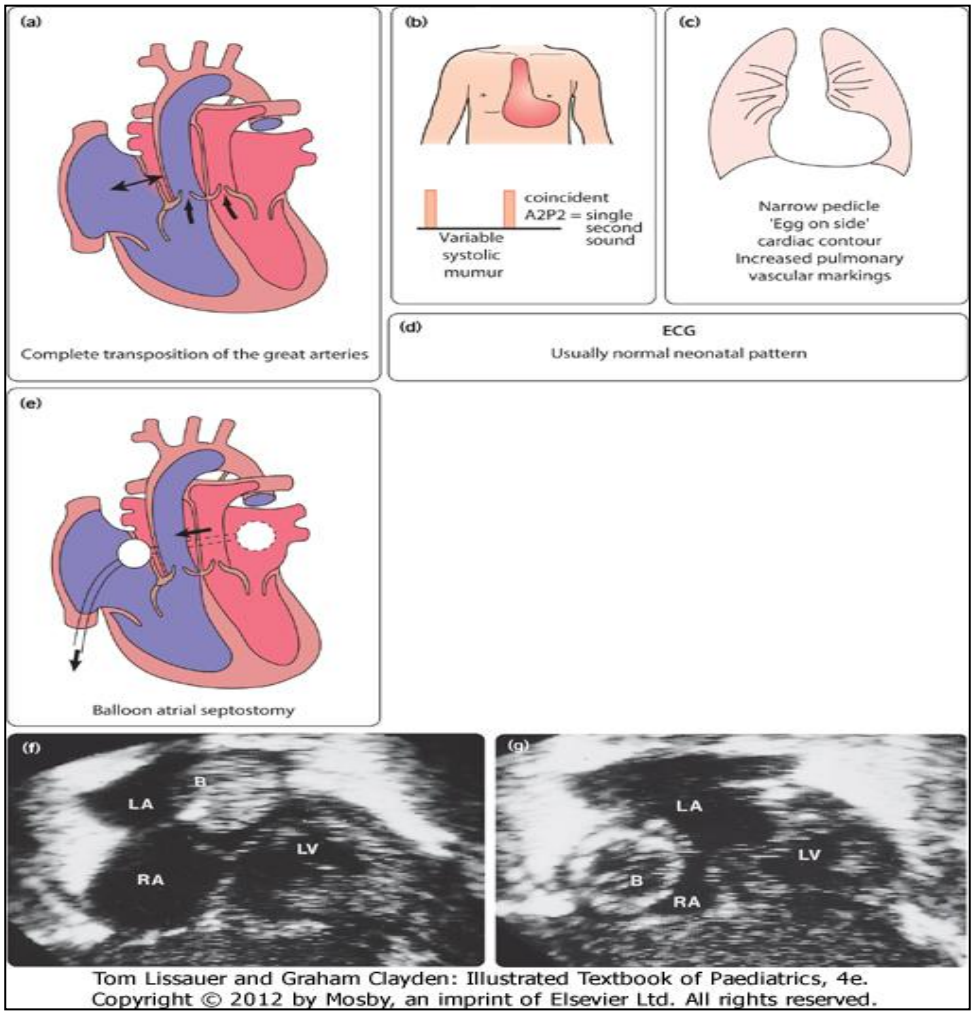


Figure 17.9 Transposition of the great arteries. (a) Transposition of the great arteries. There must be mixing of blood between the two circulations for this to be compatible with life. (b) Heart sounds. (c) Chest radiograph. (d) ECG. (e) Balloon atrial septostomy. A balloon (about 2 ml) is pulled through the atrial septum from the left atrium to the right atrium in order to increase the size of the atrial defect. This is done with echocardiographic guidance. (f) Echocardiogram showing balloon in left atrium. (g) Balloon has been pulled through the atrial septum and is now in the right atrium. (B, balloon; LA, left atrium; RA, right atrium; LV, left ventricle)

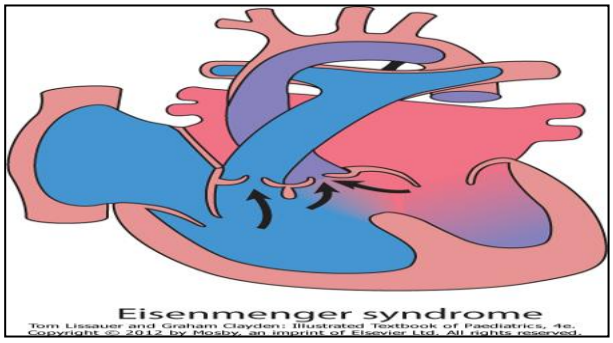


Figure 17.10 Eisenmenger syndrome with right-to-left shunting from pulmonary vascular disease following increased pulmonary blood flow and pulmonary hypertension with large VSD.

Summary
Cyanotic congenital heart disease

Lesion	Clinical features	Management
Tetralogy of Fallot	Loud murmur at ULSE	Surgery at 6-9 months
	Clubbing of fingers and toes (older) Hypercyanotic spells	
Transposition of the great arteries	Neonatal cyanosis No murmur	Prostaglandin infusion Balloon atrial septostomy
		Arterial switch operation in neonatal period
Eisenmenger syndrome	No murmur Right heart failure (late)	Medication to delay transplantation

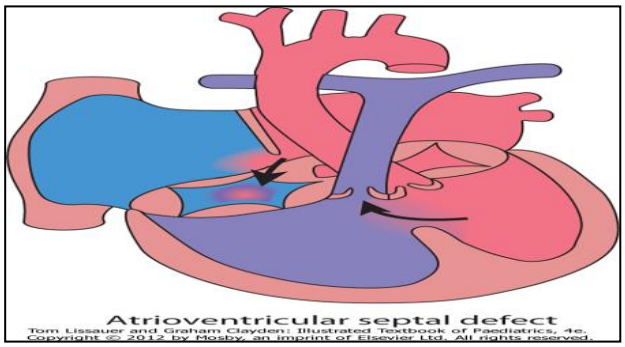


Figure 17.11 Complete atrioventricular septal defect, with a common atrioventricula valve between a large atrial and ventricular component to the AVSD.

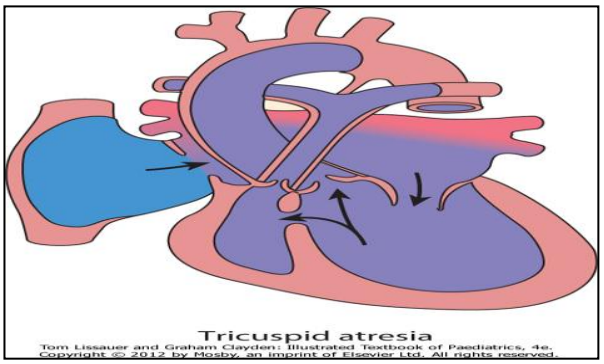


Figure 17.12 In tricuspid atresia, there is only one effective ventricle because of complete absence of the tricuspid valve.

Summary
Common mixing

Lesion	Clinical features	Management
Atrioventricular septal defect (complete)	Down syndrome (often) Cyanosis at birth	Treat heart failure medically Surgical repair at 3 months
	Breathless at 2-3 weeks of life	
Complex diseases (e.g. tricuspid atresia)	Cyanosis Breathless	Shunt (Blalock-Taussig) or pulmonary artery banding, then surgery (Fontan operation)

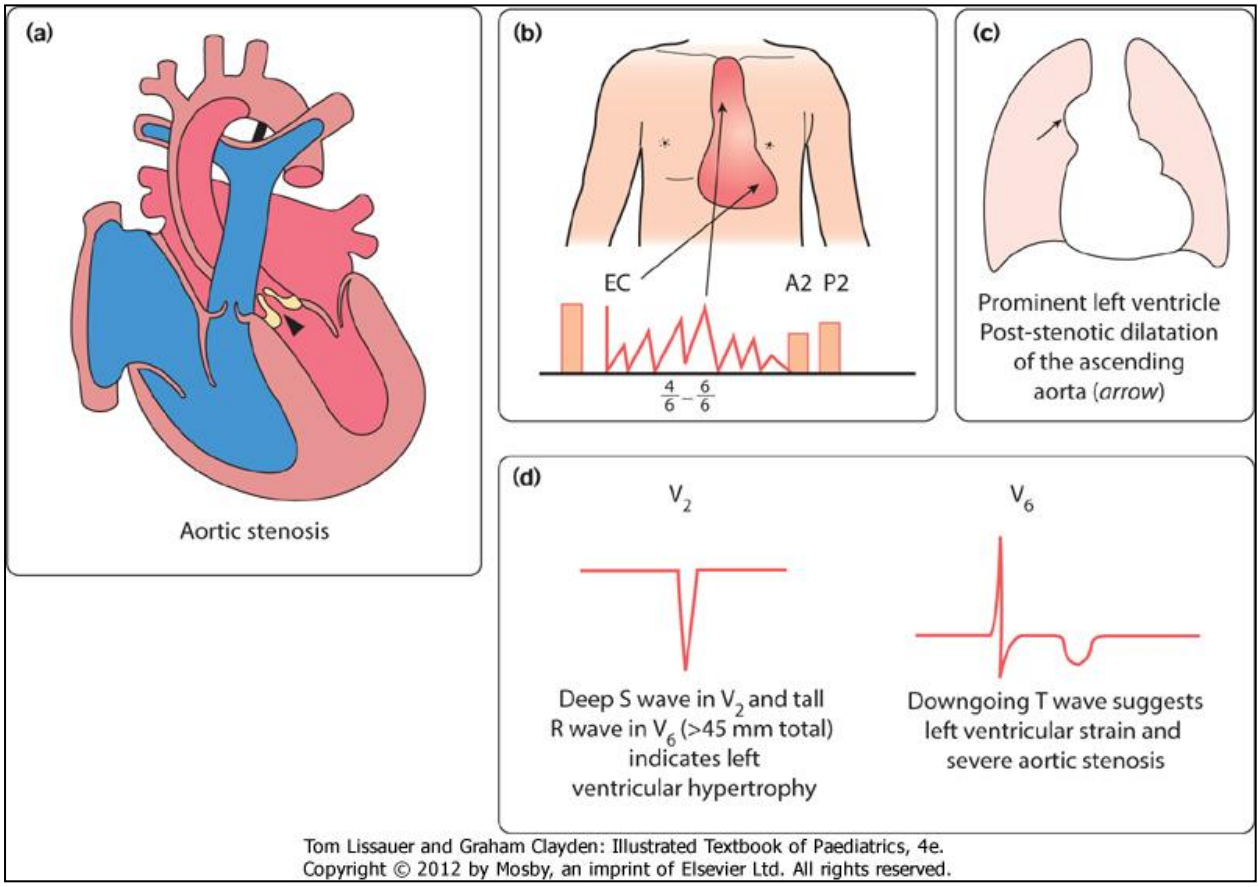


Figure 17.13 Aortic stenosis. (a) Aortic stenosis. (b) Murmur. (c) Chest radiograph. (d) ECG.

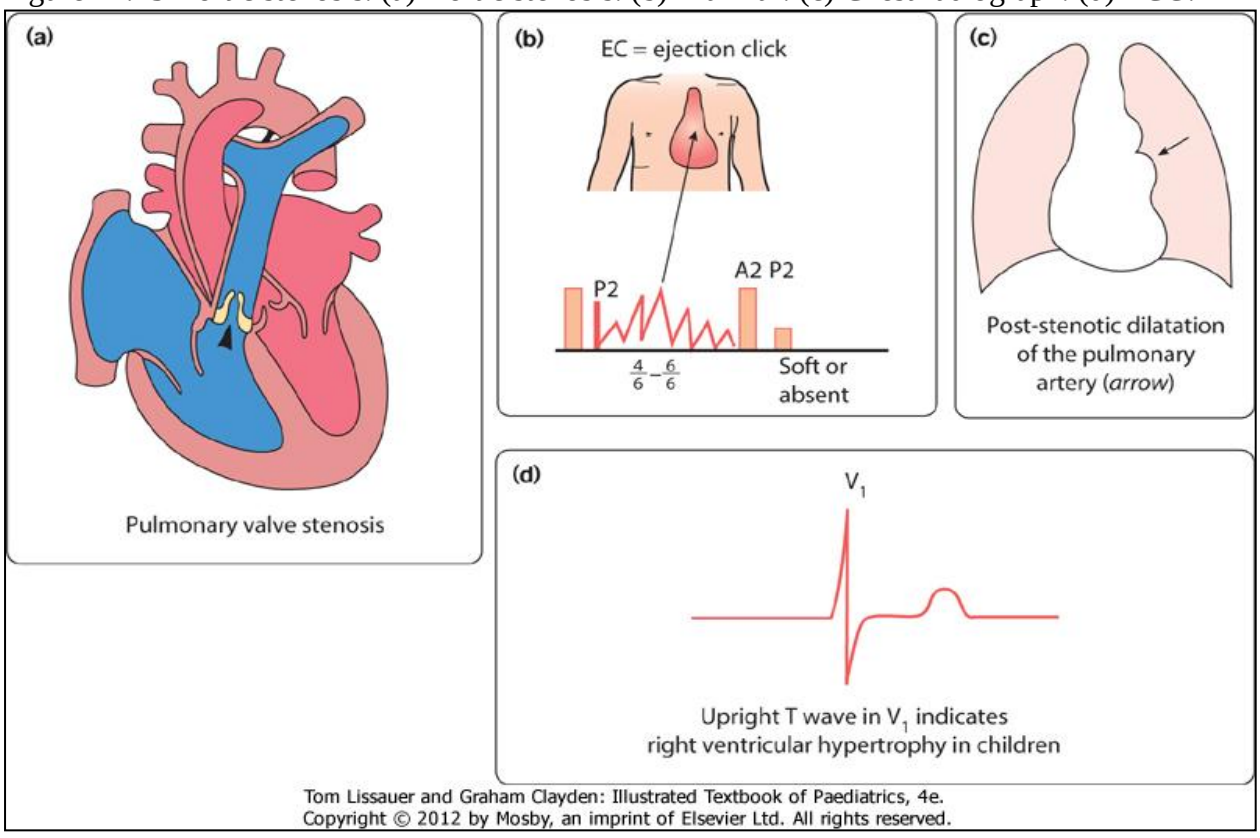


Figure 17.14 Pulmonary valve stenosis. (a) Pulmonary valve stenosis. (b) Murmur. (c) Chest radiograph. (d) ECG.

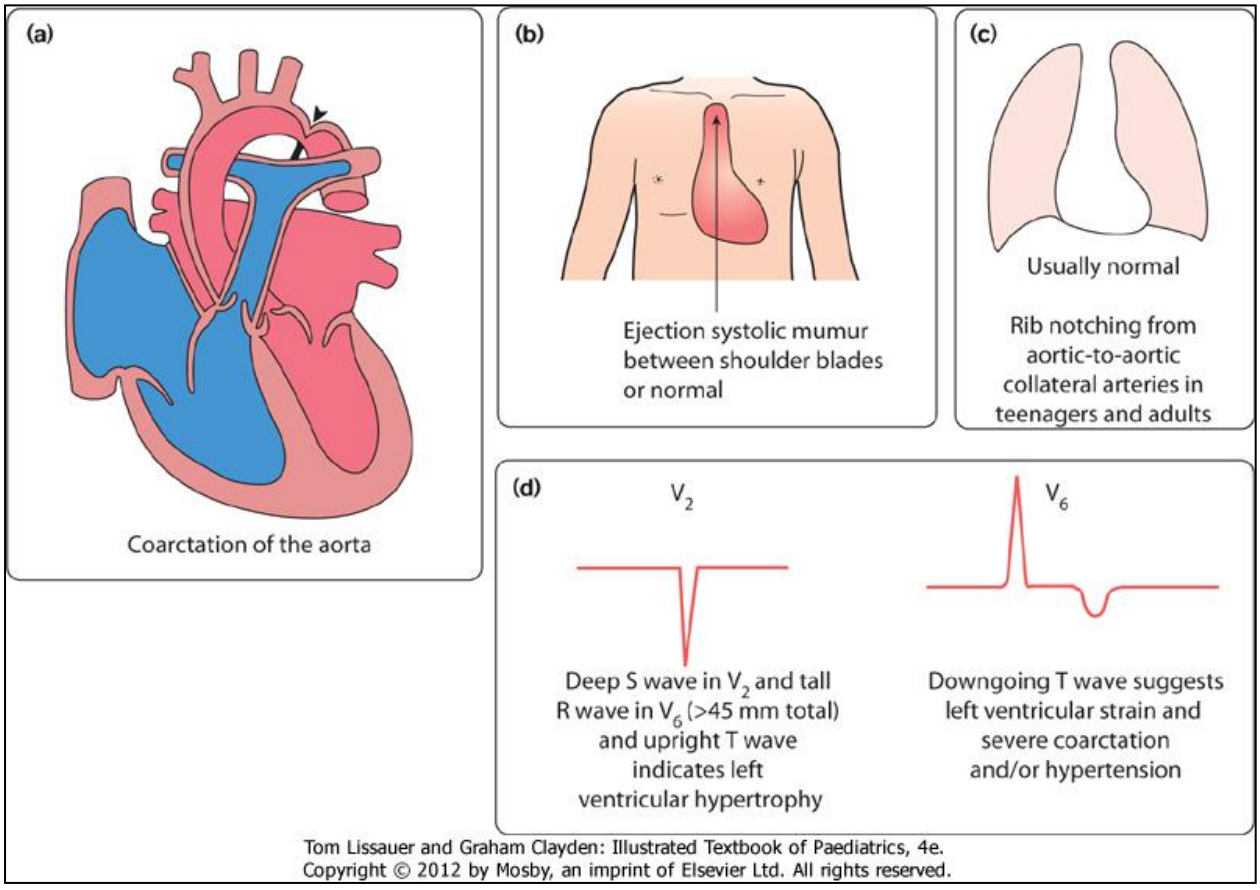


Figure 17.15 Coarctation of the aorta. (a) Coarctation of the aorta. There is narrowing of the aorta distal to the left subclavian artery adjacent to the insertion of the arterial duct. (b) Murmur. (c) Chest radiograph. (d) ECG.

Summary
Outflow obstruction in the well child

Lesion	Signs	Management
Aortic stenosis	Murmur, upper right sternal edge; carotid thrill	Balloon dilatation
Pulmonary stenosis	Murmur, upper left sternal edge; no carotid thrill	Balloon dilatation
Coarctation (adult type)	Systemic hypertension	Stent insertion or surgery
	Radio-femoral delay	

Summary
Left heart outflow obstruction in the sick infant - duct-dependent lesions

Lesion	Clinical features	Management
Coarctation of the aorta	Circulatory collapse	Maintain ABC
	Absent femoral pulses	Prostaglandin infusion
Interruption of the aortic arch	Circulatory collapse Absent femoral pulses and absent left brachial pulse	Maintain ABC Prostaglandin infusion
Hypoplastic left heart syndrome	Circulatory collapse All peripheral pulses absent	Maintain ABC Prostaglandin infusion

Jones criteria for diagnosis of rheumatic fever

Required to make the diagnosis

Two major, or one major and two minor, criteria plus supportive evidence of preceding group A streptococcal infection (markedly raised ASO titre or other streptococcal antibodies, or group A streptococcus on throat culture)

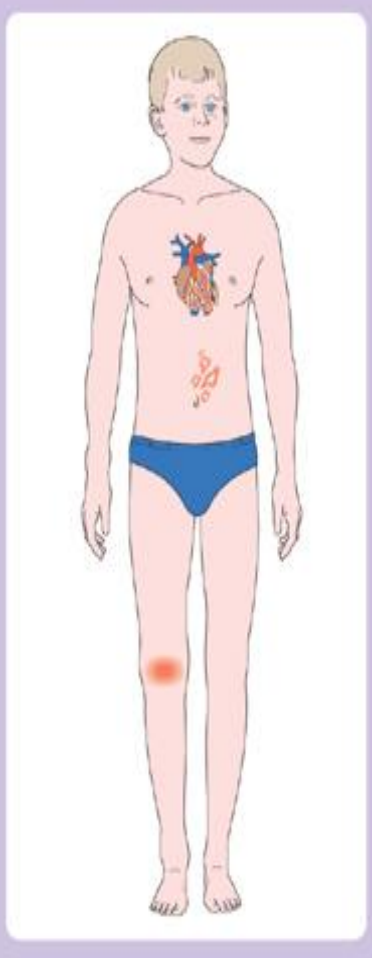
Major manifestations

Pancarditis (50%)
Endocarditis
- significant murmur
- valvular dysfunction

Myocarditis
- may lead to heart failure and death

Pericarditis
- pericardial friction rub
- pericardial effusion
- tamponade

Polyarthritis (80%)
Ankles, knees and wrists
Exquisite tenderness, moderate redness and swelling
'Flitting', lasting <1 week in a joint, but migrating to other joints over 1–2 months



Sydenham chorea (10%)
2–6 months after the streptococcal infection
Involuntary movements and emotional lability for 3–6 months

Erythema marginatum (<5%)
Uncommon, early manifestation
Rash on trunk and limbs
Pink macules spread outwards, causing pink border with fading centre. Borders may unite to give a map-like outline

Subcutaneous nodules (rare)
Painless, pea-sized, hard
Mainly on extensor surfaces

Minor manifestations

Fever
Polyarthralgia
History of rheumatic fever
Raised acute-phase reactants: ESR, C-reactive protein, leucocytosis
Prolonged P–R interval on ECG

Chapter 18: Kidney and urinary tract disorders

Box 18.1 Presentation of UTI in infants and children

Infants

- Fever
- Vomiting
- Lethargy or irritability
- Poor feeding/failure to thrive
- Jaundice
- Septicaemia
- Offensive urine
- Febrile convulsion (>6 months).

Children

- Dysuria and frequency
- Abdominal pain or loin tenderness
- Fever with or without rigors (exaggerated shivering)
- Lethargy and anorexia
- Vomiting, diarrhoea
- Haematuria
- Offensive/cloudy urine
- Febrile convulsion
- Recurrence of enuresis.

Table 18-3. Methods and interpretation of dipstick testing in children

Methods of dipstick testing	
Nitrite stick testing	Positive result useful as very likely to indicate a true UTI But some children with a UTI are nitrite-negative
Leucocyte esterase stick testing (for WBCs)	May be present in children with UTI but may also be negative Present in children with febrile illness without UTIs Positive in balanitis and vulvovaginitis
Interpretation of results	
Leucocyte esterase and nitrite positive	Regard as UTI
Leucocyte esterase negative and nitrite positive	Start antibiotic treatment Diagnosis depends on urine culture
Leucocyte esterase positive and nitrite negative	Only start antibiotic treatment if clinical evidence of UTI Diagnosis depends on urine culture
Leucocyte esterase and nitrite negative	UTI unlikely. Repeat or send urine for culture if clinical history suggests UTI
Blood, protein, and glucose present on stick testing	Useful in any unwell child to identify other diseases, e.g. nephritis, diabetes mellitus, but will not discriminate between children with and without UTIs

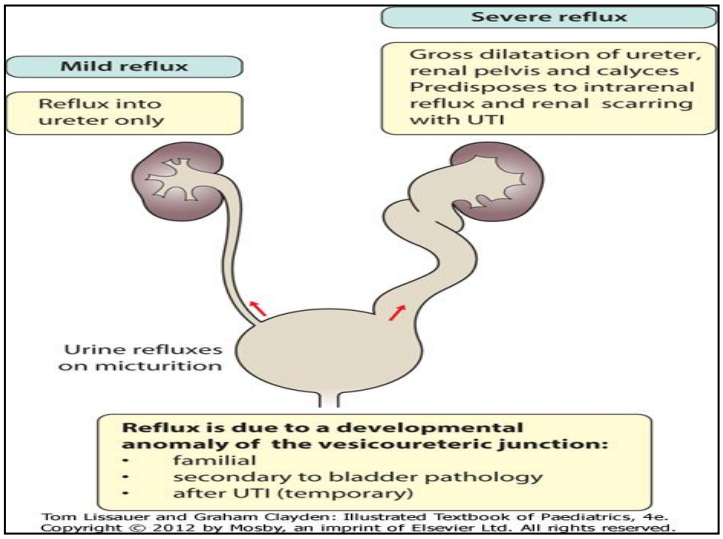


Figure 18.12 Vesicoureteric reflux

Case History 18.2 Urinary tract infection

Jack, a 2-month-old infant, stopped feeding and had a high, intermittent fe
was referred to hospital, where he had an infection screen. Urine examina
showed >100 white blood cells, >10^5 *E. coli*/ml. He was treated with intra
antibiotics. An ultrasound showed that the left kidney was smaller than th
kidney with dilated ureters. He was started on prophylactic antibiotics. A
scan (Fig. 18.14) performed 3 months later confirmed bilateral renal scarri
the left kidney contributing 33% of renal function. The MCUG (Fig. 18.15)
bilateral vesicoureteric reflux. At 4 years of age, the reflux had resolved ar
antibiotic prophylaxis was stopped. His blood pressure and renal growth a
function continue to be monitored.

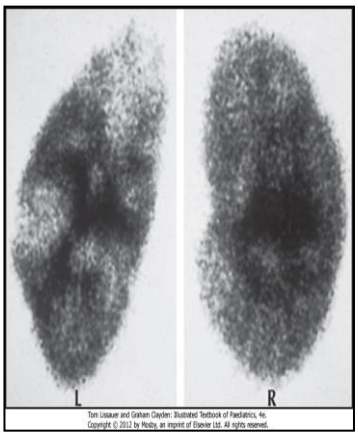
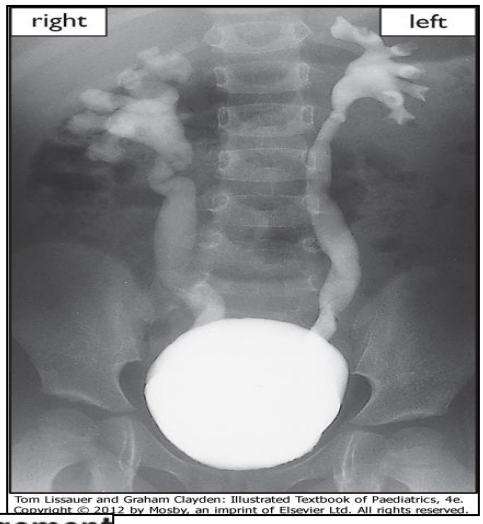


Figure 18.14 DMSA scan showing bilateral renal scarring, more severe on left upper pole.

Figure 18.15 Micturating cystourethrogram showing bilateral vesicoureteric reflux with ureteric dilatation and dilated, clubbed calyces on the right.



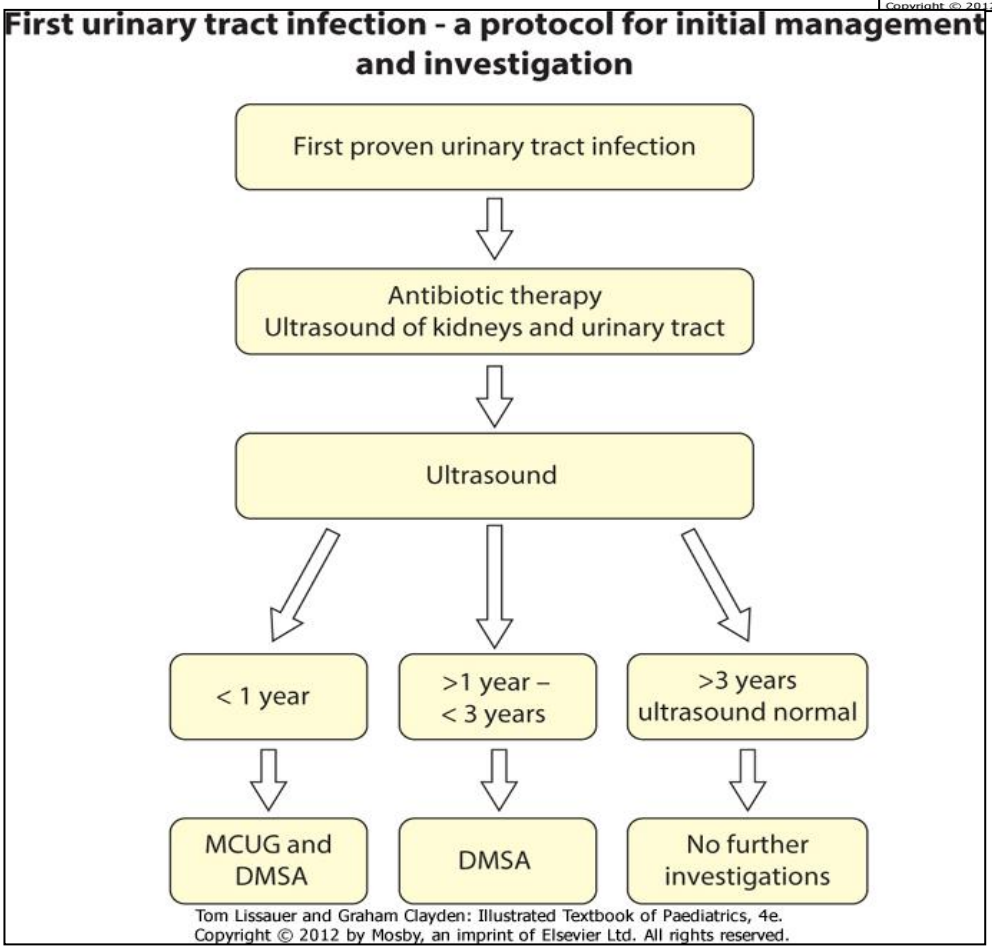


Figure 18.13 An example of a protocol for the initial management and investigation of a first urinary tract infection. This is a controversial area. The UK NICE guidelines, 2007 do not recommend ultrasound examination for first UTI if there was response to antibiotic treatment within 48 h, unless 6 months old or atypical or recurrent, but many paediatric nephrologists consider this approach too conservative and follow protocols like the one shown here.

A child with a first urinary tract infection

Why important?
Up to half have a structural abnormality of their urinary tract
Pyelonephritis may damage the growing kidney by forming a renal scar, which may result in hypertension and chronic renal failure

Diagnosis secure?
- Suggestive clinical features?
- Upper or lower urinary tract infection?
- Urine sample properly collected and processed?
- Culture of single organism >10^5/ml if clean catch or mid-stream urine or else any organisms on suprapubic aspirate or catheter sample?

Predisposing factors?
Incomplete bladder emptying
Constipation
Vesicoureteric reflux

Why investigate?
To identify serious structural abnormalities, urinary obstruction, renal scars, vesicoureteric reflux.

What investigation?
Consider:
- Ultrasound of kidneys and urinary tract
- DMSA to check for renal scars 3 months after UTI
- MAG3 or MCUG to detect obstruction and vesicouretic reflux.

Management
Treat infection with antibiotics
Advice about medical preventative measures:
- High fluid intake
- Regular voiding, double micturition
- Prevent or treat constipation
- Good perineal hygiene
- *Lactobacillus acidophilus*

Advise to check urine culture if develops clinical features suggestive of non-specific illness

If renal scarring or reflux on investigation, or develops recurrent UTIs:
- Consider low-dose antibiotic prophylaxis
- Monitor blood pressure, renal growth and function

Summary
Enuresis

Daytime enuresis

- Consider causes - developmental or psychogenic, bladder instability or neuropathy, urinary tract infection, constipation, ectopic ureter.

Secondary (onset) enuresis

- Consider - emotional upset, UTI, polyuria from an osmotic diuresis in diabetes mellitus or a renal concentrating disorder.

Box 18.2 Causes of proteinuria

- Orthostatic proteinuria
- Glomerular abnormalities
  - - Minimal change disease
  - - Glomerulonephritis
  - - Abnormal glomerular basement membrane (familial nephritides)
- Increased glomerular filtration pressure
- Reduced renal mass
- Hypertension
- Tubular proteinuria.

Box 18.3 Investigations performed at presentation of nephrotic syndrome

- Urine protein - on test strips ('dipstick')
- Full blood count and ESR
- Urea, electrolytes, creatinine, albumin
- Complement levels - C3, C4
- Antistreptolysin O or anti-DNAse B titres and throat swab
- Urine microscopy and culture
- Urinary sodium concentration
- Hepatitis B and C screen
- Malaria screen if travel abroad.

Summary

Nephrotic syndrome

- Clinical signs - oedema (periorbital, scrotal or vulval, leg and ankle oedema, ascites, pleural effusions)
- Diagnosis - heavy proteinuria and low plasma albumin.

Steroid-sensitive nephrotic syndrome

- Characteristic features - 1 to 10 years old, no macroscopic haematuria, and blood pressure, complement levels and renal function are normal
- Management - oral corticosteroids, renal biopsy if unresponsive or atypical features
- Complications - hypovolaemia, thrombosis, infection (pneumococcal), hypercholesterolaemia
- Prognosis - may resolve or else there may be infrequent or frequent relapse.

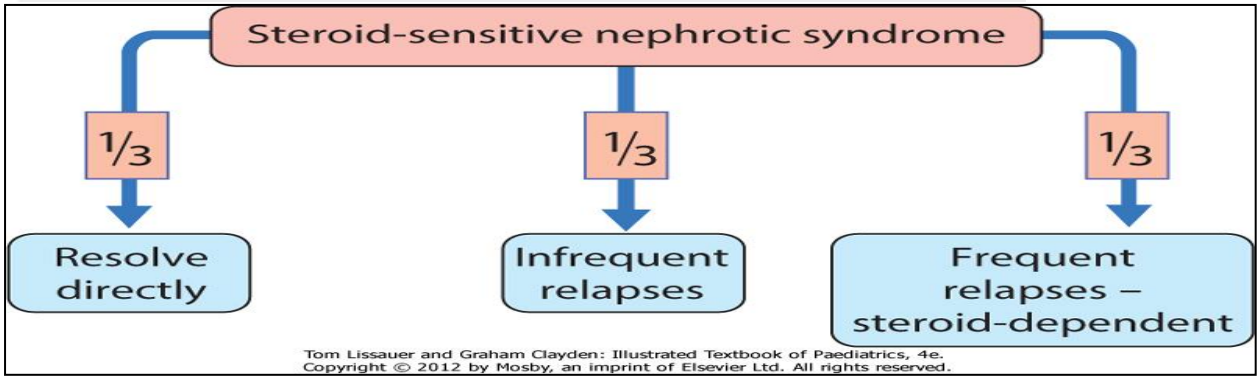


Table 18-4. Steroid-resistant nephrotic syndrome

Cause	Specific features	Prognosis
Focal segmental glomerulosclerosis	Most common Familial or idiopathic	30% progress to end-stage renal failure in 5 years; 20% respond to cyclophosphamide, ciclosporin, tacrolimus or rituximab Recurrence post-transplant is common
Mesangiocapillary glomerulonephritis (membranoproliferative glomerulonephritis)	More common in older children Haematuria and low complement level present	Decline in renal function over many years
Membranous nephropathy	Associated with hepatitis B May precede SLE	Most remit spontaneously within 5 years

Haematuria

Box 18.4 Causes of haematuria

Non-glomerular

- Infection (bacterial, viral, TB, schistosomiasis)
- Trauma to genitalia, urinary tract or kidneys
- Stones
- Tumours
- Sickle cell disease
- Bleeding disorders
- Renal vein thrombosis
- Hypercalciuria.

Glomerular

- Acute glomerulonephritis (usually with proteinuria)
- Chronic glomerulonephritis (usually with proteinuria)
- IgA nephropathy
- Familial nephritis, e.g. Alport syndrome
- Thin basement membrane disease.

Box 18.5 Investigation of haematuria

All patients

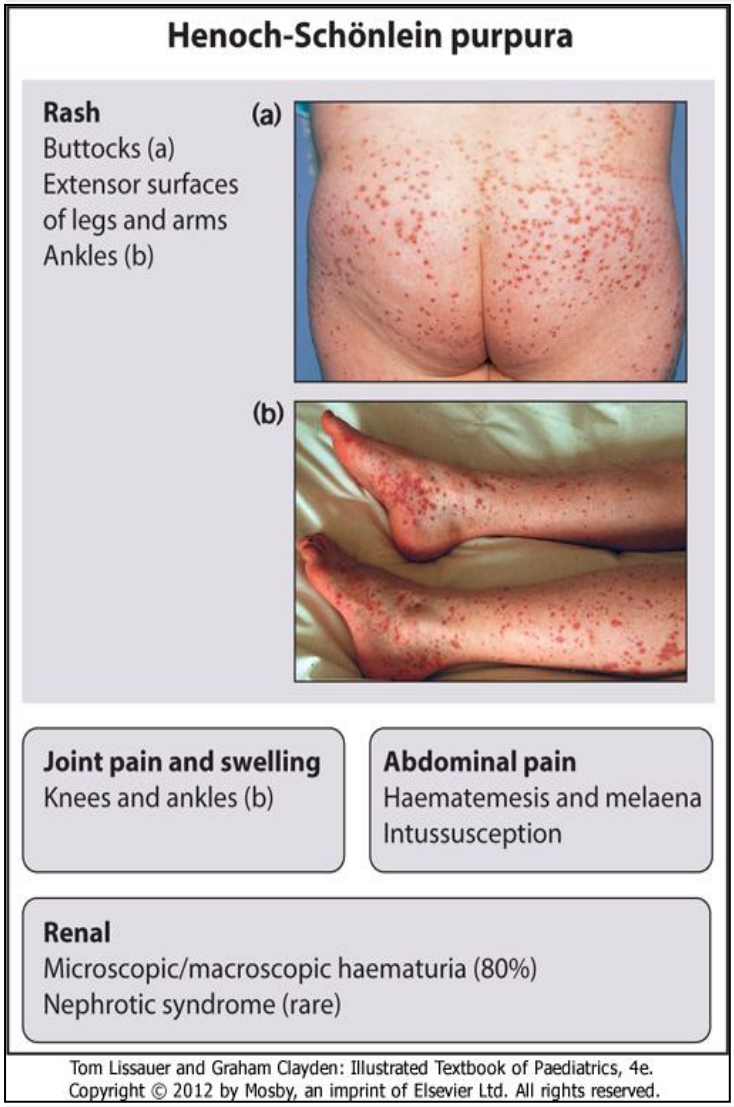
- Urine microscopy (with phase contrast) and culture
- Protein and calcium excretion
- Kidney and urinary tract ultrasound
- Plasma urea, electrolytes, creatinine, calcium, phosphate, albumin
- Full blood count, platelets, clotting screen, sickle cell screen.

If suggestive of glomerular haematuria

- ESR, complement levels and anti-DNA antibodies
- Throat swab and antistreptolysin O/anti-DNAse B titres
- Hepatitis B and C screen
- Renal biopsy if indicated
- Test mother's urine for blood (if Alport syndrome suspected)
- Hearing test (if Alport syndrome suspected).

Box 18.6 Causes of acute nephritis

- Post-infectious (including streptococcus)
- Vasculitis (Henoch-Schönlein purpura or, rarely, SLE, Wegener granulomatosis, microscopic polyarteritis, polyarteritis nodosa)
- IgA nephropathy and mesangiocapillary glomerulonephritis
- Anti-glomerular basement membrane disease (Goodpasture syndrome) - very rare.



Summary
Acute nephritis

- Cause: usually post-infectious or follows a streptococcal infection, but also vasculitis (including Henoch-Schönlein purpura), IgA nephropathy and familial nephritis
- Clinical features: oedema (around the eyes), hypertension, decreased urine output, haematuria and proteinuria
- Management: fluid and electrolyte balance, diuretics, monitor for rapid deterioration in renal function.

Box 18.7 Causes of hypertension

- **Renal**
  - - Renal parenchymal disease
  - - Renovascular, e.g. renal artery stenosis
  - - Polycystic kidney disease (ARPKD and ADPKD)
  - - Renal tumours
- **Coarctation of the aorta**
- **Catecholamine excess**
  - - Phaeochromocytoma
  - - Neuroblastoma
- **Endocrine**
  - - Congenital adrenal hyperplasia
  - - Cushing syndrome or corticosteroid therapy
  - - Hyperthyroidism
- **Essential hypertension**
  - - A diagnosis of exclusion.

Box 18.8 Causes of palpable kidneys

Unilateral

- Multicystic kidney
- Compensatory hypertrophy
- Obstructed hydronephrosis
- Renal tumour (Wilms tumour)
- Renal vein thrombosis

Bilateral

- Autosomal recessive (infantile) polycystic kidneys
- Autosomal dominant (adult) polycystic kidneys
- Tuberous sclerosis
- Renal vein thrombosis.

Box 18.9 Causes of Fanconi syndrome
Idiopathic

Secondary to inborn errors of metabolism

- Cystinosis (an autosomal recessive disorder causing intracellular accumulation of cystine)
- Glycogen storage disorders
- Lowe syndrome (oculocerebrorenal dystrophy)
- Galactosaemia
- Fructose intolerance
- Tyrosinaemia
- Wilson disease

Acquired

- Heavy metals
- Drugs and toxins
- Vitamin D deficiency.

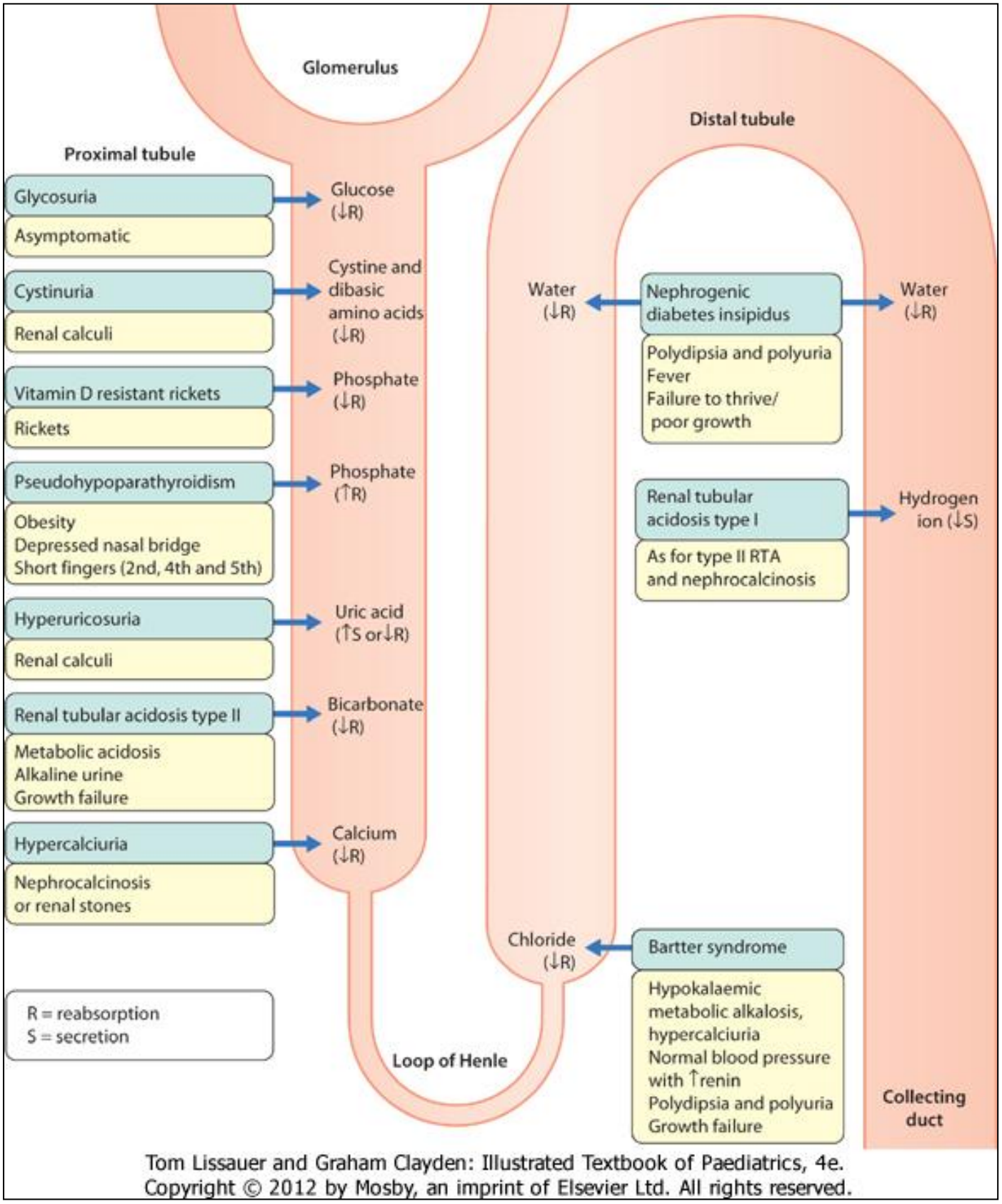


Figure 18.21 Schematic diagram of specific transport defects in some renal tubular disorders.

Box 8.10 Causes of acute renal failure

Pre renal

- Hypovolaemia:
  - - Gastroenteritis
  - - Burns
  - - Sepsis
  - - Haemorrhage
  - - Nephrotic syndrome
- Circulatory failure

Renal

- Vascular:
  - - Haemolytic uraemic syndrome (HUS)
  - - Vasculitis
  - - Embolus
  - - Renal vein thrombosis
- Tubular:
  - - Acute tubular necrosis (ATN)
  - - Ischaemic
  - - Toxic
  - - Obstructive
- Glomerular:
  - - Glomerulonephritis
- Interstitial:
  - - Interstitial nephritis
  - - Pyelonephritis

Post renal

- Obstruction:
  - - Congenital e.g. posterior urethral valves
  - - Acquired e.g. blocked urinary catheter

Table 18-5. Some metabolic abnormalities in acute renal failure and their therapy

Metabolic abnormality	Treatment
Metabolic acidosis	Sodium bicarbonate
Hyperphosphataemia	Calcium carbonate
	Dietary restriction
Hyperkalaemia	Calcium gluconate if ECG changes
	Salbutamol (nebulised or intravenous)
	Calcium exchange resin
	Glucose and insulin
	Dietary restriction
	Dialysis

- **Haemolytic uraemic syndrome (HUS) - the triad of:**
  - **Acute renal failure**
  - **Haemolytic anaemia**
  - **Thrombocytopenia.**

Summary
Acute renal failure

- Prerenal: commonest cause in children, from hypovolaemia and circulatory failure
- Renal: most often haemolytic uraemic syndrome or multisystem failure
- Postrenal: from urinary obstruction
- Management: treat underlying cause, metabolic abnormalities, dialysis if necessary.

Table 18-6. Causes of chronic renal failure

Structural malformations	40%
Glomerulonephritis	25%
Hereditary nephropathies	20%
Systemic diseases	10%
Miscellaneous/unknown	5%

Summary
Chronic renal failure

- Causes: congenital (structural malformations and hereditary nephropathies) most common
- Presentation: abnormal antenatal ultrasound, anorexia and lethargy, polydipsia and polyuria, failure to thrive/growth failure, renal rickets, hypertension, proteinuria, anaemia
- Management: diet and nasogastric or gastrostomy feeding, phosphate restriction and activated vitamin D to prevent renal osteodystrophy, salt supplements and free access to water to control salt and water balance, bicarbonate supplements to prevent acidosis, erythropoietin to prevent anaemia, growth hormone and dialysis and transplantation.

Chapter 20: Liver disorders

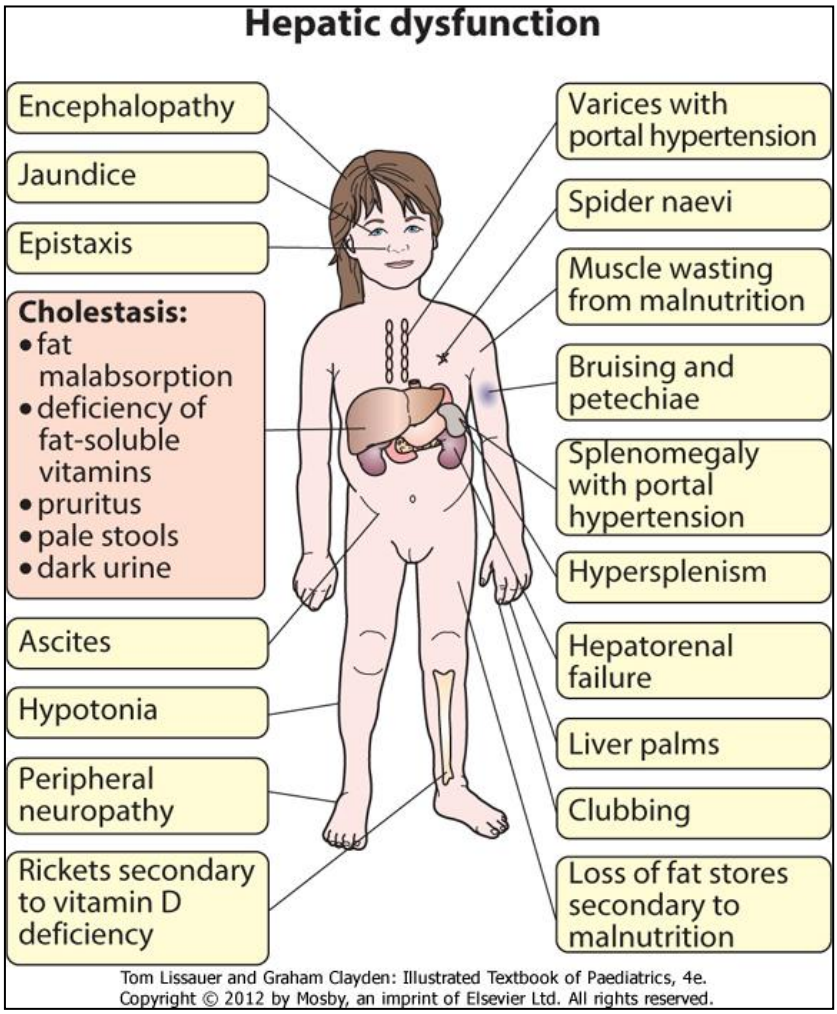


Figure 20.1 Clinical features of liver disease. In addition, these children may have growth failure and developmental delay.

Box 20.1 Causes of prolonged (persistent) neonatal jaundice

Unconjugated	Conjugated (> 20 micromol/L)
• Breast milk jaundice • Infection (particularly urinary tract) • Haemolytic anaemia, e.g. G6PD deficiency • Hypothyroidism • High gastrointestinal obstruction • Crigler-Najjar syndrome	***Bile duct obstruction*** • Biliary atresia • Choledochal cyst ***Neonatal hepatitis syndrome*** • Congenital infection • Inborn errors of metabolism • α_1-Antitrypsin deficiency • Galactosaemia • Tyrosinaemia (type 1) • Errors of bile acid synthesis • Progressive familial intrahepatic cholestasis (PFIC) • Cystic fibrosis • Intestinal failure-associated liver disease - associated with long-term parenteral nutrition ***Intrahepatic biliary hypoplasia*** • Alagille syndrome.

• In persistent neonatal jaundice, early the prognosis.

Case History 20.1 Biliary atresia

A term infant was given oral vitamin K shortly after birth. He was breast-fed. He became mildly jaundiced on the third day of life. At 5 weeks of age, he presented with poor feeding and vomiting and a history of bruising on his forehead and shoulders. His urine had become dark and stools intermittently pale. He was pale, jaundiced, had several bruises and hepatomegaly. Investigations showed:

- Hb 8.8 g/L
- Platelets 465 × 10^9/L
- Prothrombin time - 28 s (normal range 10-13 s)
- Serum bilirubin 178 micromol/L - 140 micromol/L conjugated.

The investigation of conjugated hyperbilirubinaemia is shown in Figure 20.2. The TIBIDA radionuclide scan showed no excretion at 24 h (Fig. 20.3) and a liver biopsy suggested biliary atresia (Fig. 20.4). A hepatoportoenterostomy was performed at 6 weeks of age (Fig. 20.5).

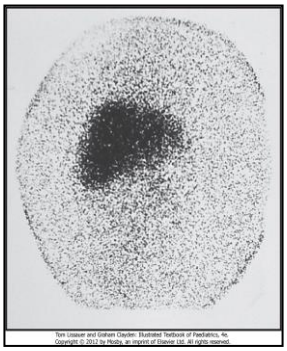


Figure 20.3 Radioisotope scan TIBIDA of liver showing good hepatic uptake of isotope and no excretion into bowel. This scan suggests extrahepatic biliary obstruction or atresia or severe intrahepatic cholestasis.

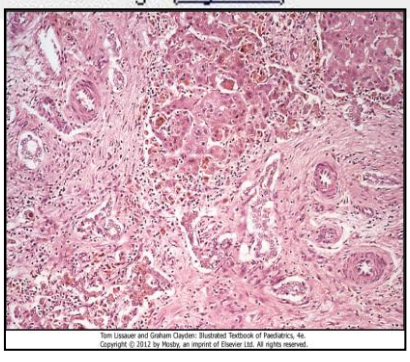
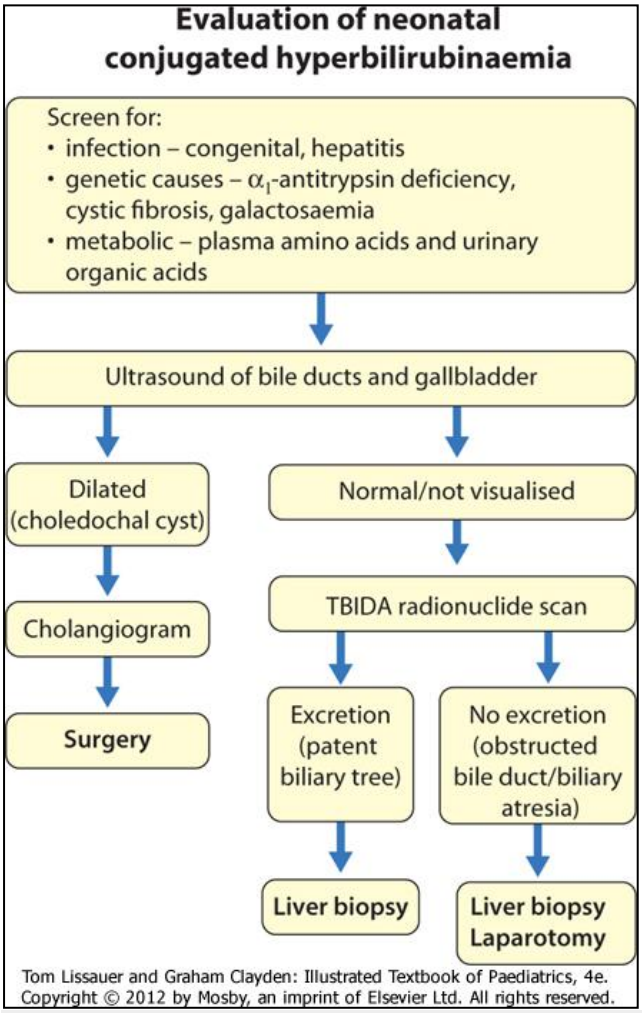


Figure 20.4 Liver biopsy of biliary atresia showing bands of fibrous tissue with bile duct proliferation

Figure 20.5 Shortly after successful bile drainage by hepatoportoenterostomy (Kasai procedure) for biliary atresia.



Box 20.2 Causes of chronic liver disease in children

- Chronic hepatitis
- Post-viral hepatitis B, C
- Autoimmune hepatitis
- Drugs (nitrofurantoin, non-steroidal anti-inflammatory)
- Inflammatory bowel disease
- Primary sclerosing cholangitis (± ulcerative colitis)
- Wilson disease (>3 years)
- α_1-Antitrypsin deficiency
- Cystic fibrosis
- Neonatal liver disease
- Bile duct lesions.

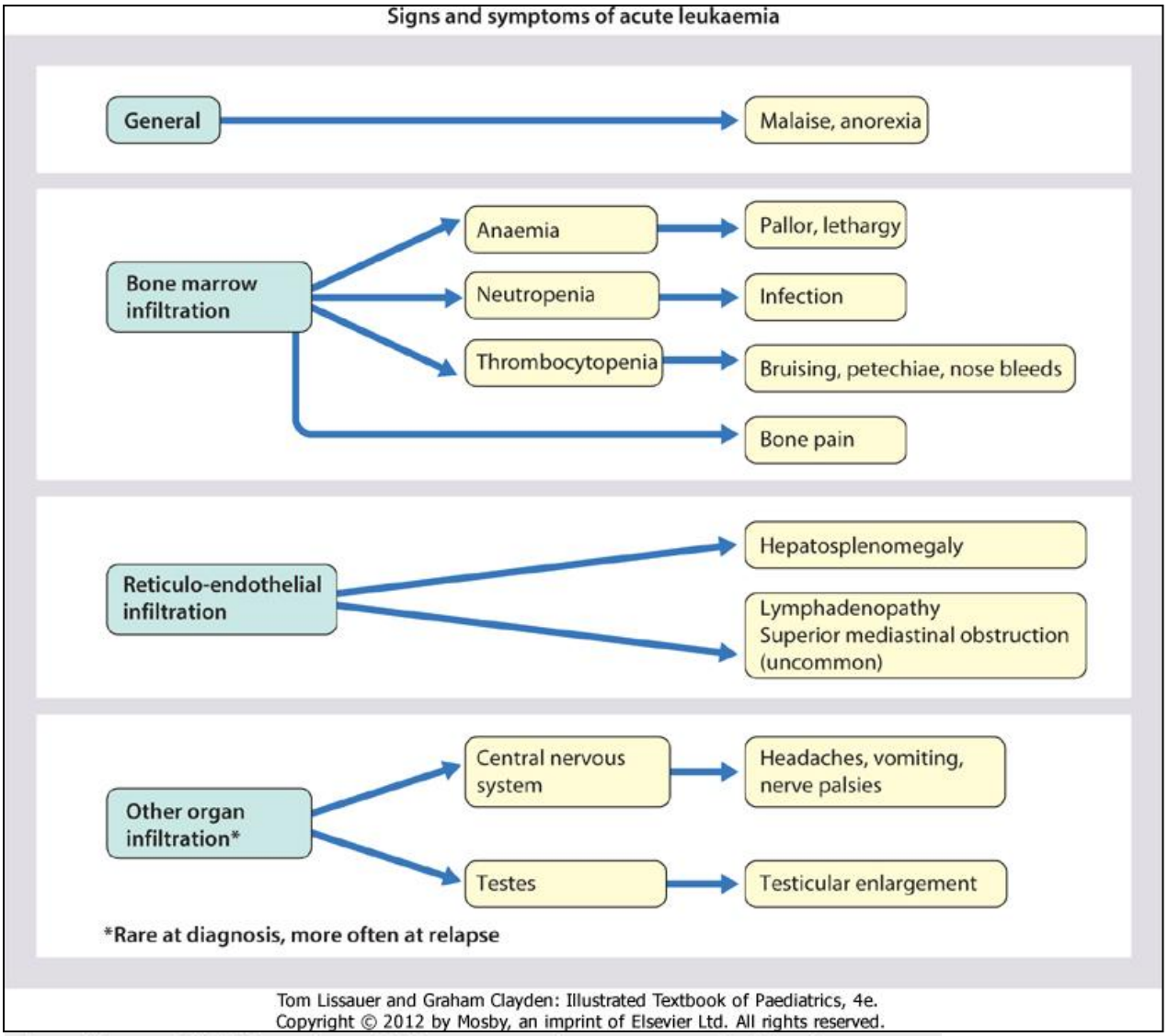
Summary
Hepatitis B virus (HBV)

- Perinatal transmission from carrier mothers should be prevented by maternal screening and giving the infant a course of hepatitis B vaccine with hepatitis B immunoglobulin if indicated
- Infection may result in chronic HBV liver disease, which may progress to cirrhosis and hepatocellular carcinoma.

Table 20-1. Causes of acute liver failure in children

Infection	Viral hepatitis A, B, C, non-A to G
Poisons/drugs	Paracetamol, isoniazid, halothane, *Amanita phalloides* (poisonous mushroom)
Metabolic	Wilson disease, tyrosinaemia
Autoimmune hepatitis	
Reye syndrome	

Chapter 21: Malignant disease



Case History 21.1 Disseminated disease, e.g. bone marrow infiltration, causing systemic ill-health

A 4-year-old girl was generally unwell, lethargic, looking pale and occasionally febrile over a period of 9 weeks. Two courses of antibiotics for recurrent sore throat failed to result in any benefit. Her parents returned to their general practitioner when she developed a rash. Examination showed pallor, petechiae, modest generalised lymphadenopathy and mild hepatosplenomegaly. A full blood count showed:

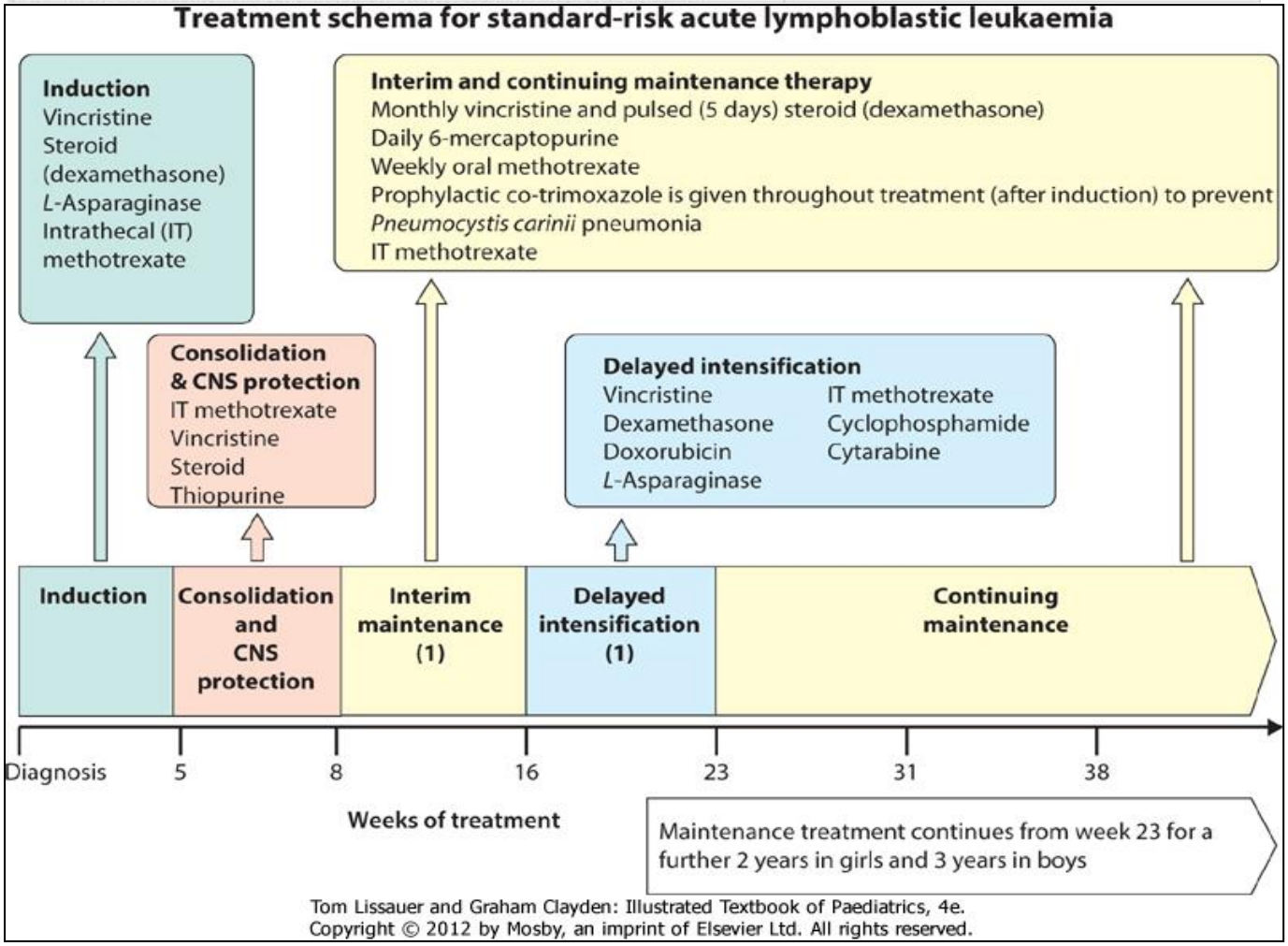
- Hb 8.3 g/dl
- WBC 15.6 × 10^9/L
- Platelets 44 × 10^9/L.

Blast cells were seen on the peripheral blood film. Cerebrospinal fluid (CSF) examination was normal. Bone marrow examination confirmed acute lymphoblastic leukaemia (Fig. 21.6).

Diagnosis: Acute lymphoblastic leukaemia.

Table 21-1. Prognostic factors in acute lymphatic leukaemia

Prognostic factor	High-risk features
Age	<1 year or >10 years
Tumour load (measured by the white cell count, WBC)	$>50 \times 10^9$/L
Cytogenetic/molecular genetic abnormalities in tumour cells	e.g. MLL rearrangement, t(4;11), hypodiploidy (<44 chromosomes)
Speed of response to initial chemotherapy	Persistence of leukaemic blasts in the bone marrow
Minimal residual disease assessment (MRD) (submicroscopic levels of leukaemia detected by PCR)	High



Chapter 22: hematological disorders

Haemoglobin type	Globin chains α-gene cluster	β-gene cluster
Embryonic		
Hb Gower 1	ξ_2	E_2
Hb Gower 2	α_2	E_2
Hb Portland	ξ_2	γ_2
Fetal		
HbF	α_2	γ_2
Adult		
HbA	α_2	β_2
HbA_2	α_2	δ_2
Haemoglobin types in newborns and adults		
Newborn	HbF 74%, HbA 25%, HbA_2 1%	
Children >1 year old and adults	HbA 97%, HbA_2 2%	

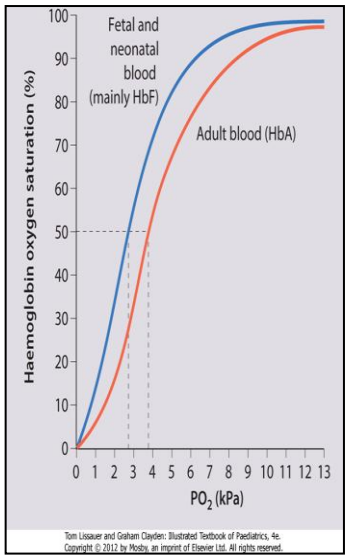


Figure 22.1 Oxygen dissociation curve showing the left shift of HbF compared with HbA. HbF-containing red cells have a higher affinity for oxygen and hold on to oxygen, delivering less to the tissues.

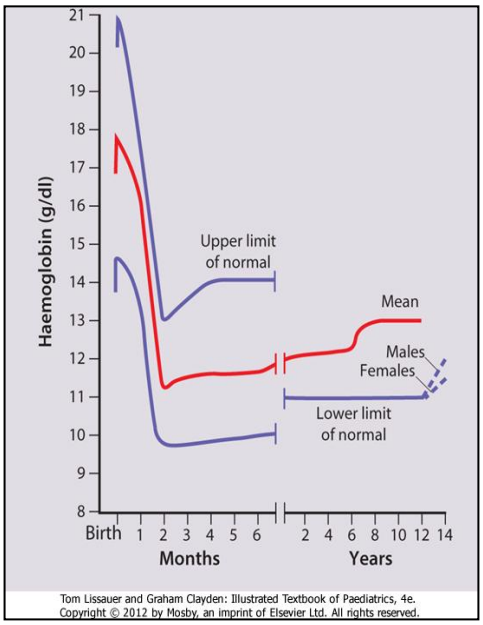


Figure 22.2 Changes in haemoglobin concentration with age, showing that the haemoglobin is high at birth, falling to its lowest concentration at 2-3 months of age

Summary
Haemoglobin at birth

- The Hb concentration is high at birth (>14 g/dl) but falls to its lowest level at 2 months of age.
- Fetal Hb (HbF) is gradually replaced by adult Hb (HbA + HbA_2) during infancy.

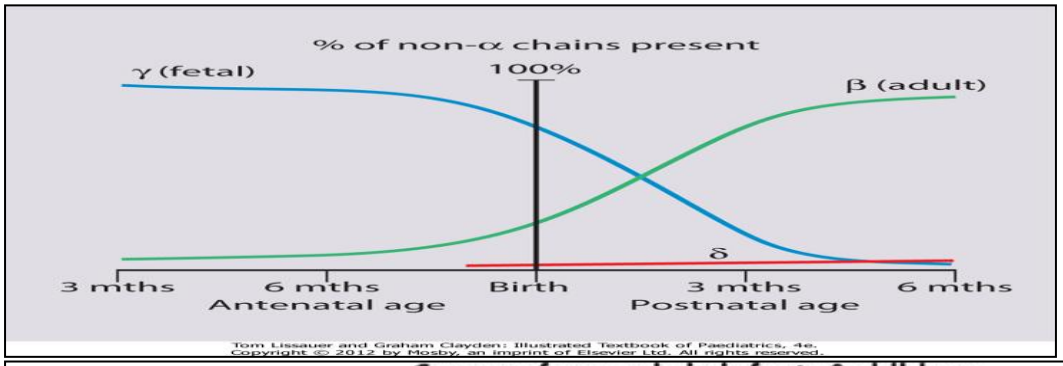
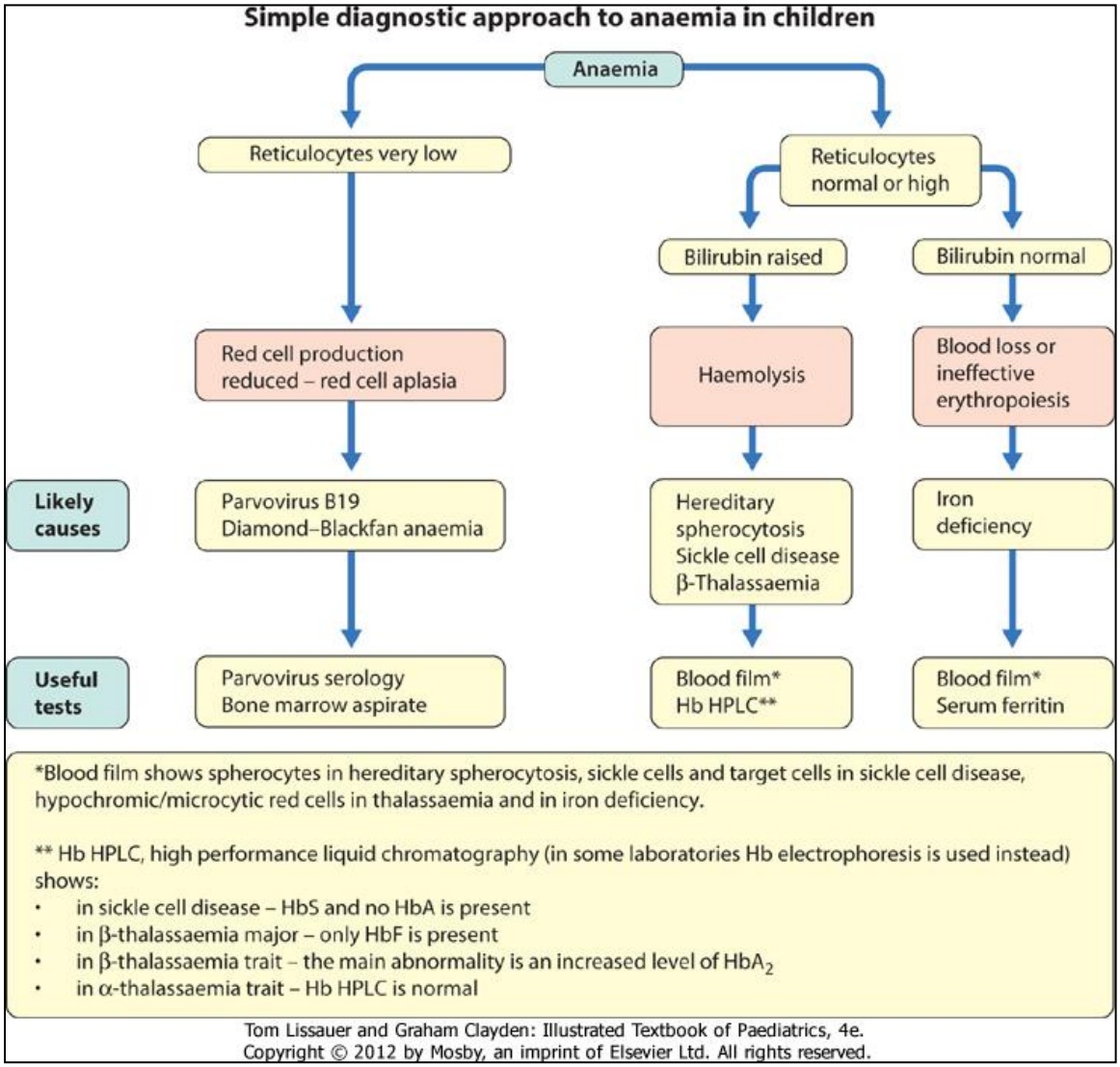


Figure 22.7 Changes in haemoglobin chains in the fetus and infancy.

Causes of anaemia in infants & children

Impaired red cell production	Red cell aplasia	Parvovirus B19 infection Diamond–Blackfan anaemia (congenital red cell aplasia) Transient erythroblastopenia of childhood Rarities: Fanconi anaemia, aplastic anaemia, leukaemia
	Ineffective erythropoiesis	Iron deficiency Folic acid deficiency Chronic inflammation (juvenile idopathic arthritis) Chronic renal failure Rarities: myelodysplasia, lead poisoning
Increased red cell destruction (haemolysis)	Red cell membrane disorders	Hereditary spherocytosis
	Red cell enzyme disorders	Glucose-6-phosphate dehydrogenase deficiency
	Haemoglobinopathies	Thalassaemias, sickle cell disease
	Immune	Haemolytic disease of the newborn Autoimmune haemolytic anaemia
Blood loss	Fetomaternal bleeding	
	Chronic gastrointestinal blood loss	Meckel diverticulum
	Inherited bleeding disorders	von Willebrand disease



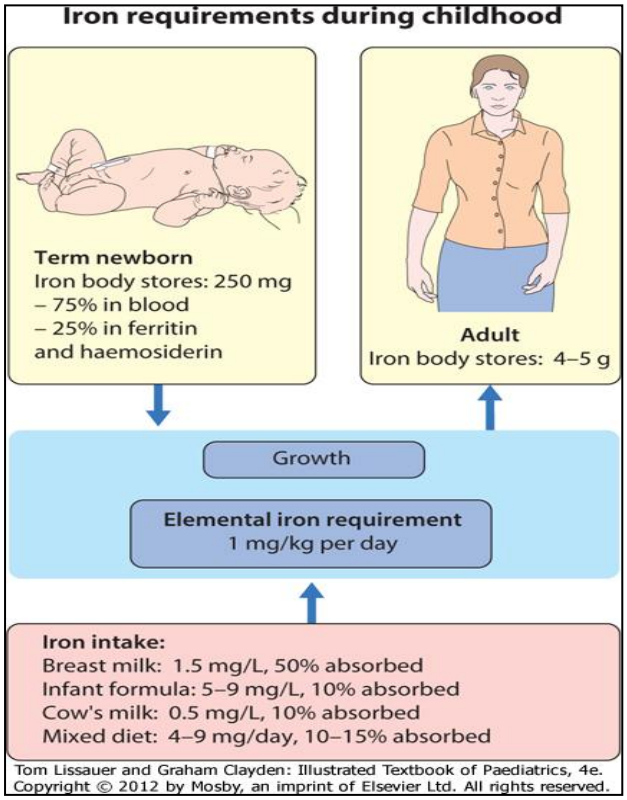
Box 22.1 Dietary sources of iron

High in iron
- Red meat - beef, lamb
- Liver, kidney
- Oily fish - pilchards, sardines, etc.

Average iron
- Pulses, beans and peas
- Fortified breakfast cereals with added vitamin C
- Wholemeal products
- Dark green vegetables - broccoli, spinach, etc.
- Dried fruit - raisins, sultanas
- Nuts and seeds - cashews, peanut butter, etc.

Foods to avoid in excess in toddlers
- Cow's milk
- Tea: tannin inhibits iron uptake
- High-fibre foods: phytates inhibit iron absorption.

• Infants should not be fed unmodified cow's milk as its iron content is low and poorly absorbed.



Case History 22.1 Iron deficiency anaemia

Ayesha, aged 2 years, was noted to look pale when she attended her general practitioner for an upper respiratory tract infection. A blood count showed Hb 5.0 g/dl, MCV 54 fl (normal 72-85 fl) and MCH 16 (normal 24-39 pg). She was drinking 3 pints of cow's milk per day and was a very fussy eater, refusing meat. She had started eating soil when playing in the garden.

Because of the inappropriately large volume of milk she was drinking, she was not sufficiently hungry to eat solid food. Replacing some of the milk with iron-rich food and treatment with oral iron produced a rise in the Hb to 7.5 g/dl within 4 weeks. Her pica (eating non-food materials) stopped. Oral iron was continued until her Hb had been normal for 3 months.

Box 22.2 Drugs and chemicals which can cause haemolysis in children with G6PD deficiency

Antimalarials
- Primaquine
- Quinine
- Chloroquine

Antibiotics
- Sulphonamides (including co-trimoxazole)
- Quinolones (ciprofloxacin, nalidixic acid)
- Nitrofurantoin

Analgesics
- Aspirin (in high doses)

Chemicals
- Naphthalene (mothballs)
- Divicine (fava beans - also called broad beans)

Table 22-2. Haemoglobins in haemoglobinopathies

	HbA	HbA_2	HbF	HbS
Newborn	25%	1%	74%	-
Adult	97%	2%	-	-
β-Thalassaemia trait	>90%	↑	+ ↑	-
β-Thalassaemia major	-	↑	↑	-
Sickle cell trait	√	√	+ ↑	√
Sickle cell disease	-	√	+ ↑	√

Clinical manifestations of sickle cell disease

Anaemia → All have moderate anaemia (usually Hb 6–10 g/dl) with clinically detectable jaundice from chronic haemolysis

Infection → All have marked increase in susceptibility to infection from encapsulated organisms such as pneumococci and *Haemophilus influenzae*. There is also an increased incidence of osteomyelitis caused by *Salmonella* and other organisms. This susceptibility to infection is due to **hyposplenism** secondary to chronic sickling and **microinfarction** in the spleen in infancy. The risk of overwhelming sepsis is greatest in early childhood

Painful crises → **Vaso-occlusive crises** causing pain affect many organs of the body with varying frequency and severity. A common mode of presentation in late infancy is the hand-foot syndrome, in which there is dactylitis with swelling and pain of the fingers and/or feet from vaso-occlusion (Fig. 22.9).
The bones of the limbs and spine are the most common sites. The most serious type of painful crisis is actute chest syndrome, which can lead to severe hypoxia and the need for mechanical ventilation and emergency transfusion. Avascular necrosis of the femoral heads may also occur. Acute vaso-occlusive crises may be precipitated by exposure to cold, dehydration, excessive exercise or stress, hypoxia or infection

Acute anaemia → Sudden drop in haemoglobin from:
Haemolytic crises – sometimes associated with infection
Aplastic crises – haemoglobin may fall precipitously. Parvovirus infection causes complete, though temporary, cessation of red blood cell production
Sequestration crises – sudden splenic or hepatic enlargement, abdominal pain and circulatory collapse from accumulation of sickled cells in spleen

Priapism → Needs to be treated promptly with exchange transfusion as it may lead to fibrosis of the corpora cavernosa and subsequent erectile impotence

Splenomegaly → Common in young children, but becomes much less frequent in older children

Long-term problems →
Short stature and delayed puberty
Stroke and cognitive problems – although 1 in 10 children with sickle cell disease have a stroke, twice that number develop more subtle neurological damage (Fig. 22.10), often manifest with poor concentration and school performance
Adenotonsillar hypertrophy – causing sleep apnoea syndrome leading to nocturnal hypoxaemia, which can cause vaso-occlusive crises and/or stroke
Cardiac enlargement – from chronic anaemia
Heart failure – from uncorrected anaemia
Renal dysfunction – may exacerbate enuresis because of inability to concentrate urine
Pigment gallstones – due to increased bile pigment production
Leg ulcers – uncommon in children
Psychosocial problems – difficulties with education and behaviour exacerbated by time off school may occur

Case History 22.2 Acute sickle chest syndrome

Princess, a 9-year-old girl with known sickle cell anaemia (HbSS), presented with increasing chest pain for 6 h. She had a non-productive cough. On examination, she had a fever of 39.7°C. Her breathing was laboured, respiratory rate increased and there was reduced air entry at both bases.

Investigations

- Haemoglobin 6 g/dl, WBC 14 × 10^9/L, platelets 350 × 10^9/L
- Chest X-ray (see Fig. 22.11)
- Oxygen saturation - 89% in air
- Arterial PO_2 - 9.3 kPa (70 mmHg) breathing face-mask oxygen
- Blood cultures were taken and viral titres performed.

A diagnosis of acute sickle chest syndrome was made, a potentially fatal condition. She was given oxygen by CPAP (continuous positive airways pressure). An exchange transfusion was performed. Broad-spectrum antibiotics were commenced. She responded well to treatment.

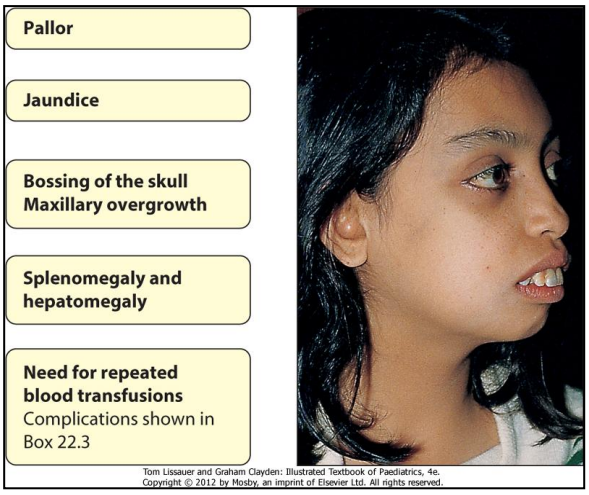


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Figure 22.13 Facies in β-thalassaemia showing maxillary overgrowth and skull bossing in a child who has not been adequately transfused. This is now very rare in the UK and developed countries.

Box 22.3 Complications of long-term blood transfusion in children

Iron deposition - the most important (all patients)
- Heart - cardiomyopathy
- Liver - cirrhosis
- Pancreas - diabetes
- Pituitary gland - delayed growth and sexual maturation
- Skin - hyperpigmentation

Antibody formation (10% of children)
- Allo-antibodies to transfused red cells in the patient make finding compatible blood very difficult

Infection - now uncommon (<10% of children)
- Hepatitis A, B, C
- HIV
- Malaria
- Prions (e.g. new variant CJD)

Venous access (common problem)
- Often traumatic in young children
- Central venous access device (e.g. Portacath) may be required; these predispose to infection.

Anaemia

Reduced red cell production

Iron deficiency anaemia
- Common in infants and toddlers, especially if of Indian subcontinent origin
- Usually dietary in origin
- Occurs because of high iron requirement (1 mg/kg/day) for growth and body stores
- Will occur if infants are weaned at 6 months of age on to a mixed diet including iron-rich food
- Is diagnosed from a hypochromic microcytic anaemia and low serum ferritin
- Is treated with dietary advice and oral iron therapy for at least 3 months

Red cell aplasia
- Congenital red cell aplasia ('Diamond–Blackfan anaemia')
- Transient erythroblastopenia of childhood (TEC)
- Parvovirus B19 infection

Increased red cell production (haemolysis)

Hereditary spherocytosis
- Inheritance is autosomal dominant, but in 25% of cases there is no family history
- May cause early, severe jaundice in newborn infants
- Is often asymptomatic, but it may cause anaemia, jaundice, splenomegaly, aplastic crisis and gallstones
- Can usually be diagnosed from the blood film
- Treatment is with folic acid, splenectomy if symptomatic

β-Thalassaemia major
- Mutation of the β-globin gene results in an inability to produce HbA ($\alpha_2\beta_2$)
- Clinical features: severe anaemia, failure to thrive/ growth failure and hepatosplenomegaly
- Condition is fatal without regular blood transfusions, but blood transfusions cause iron overload
- Iron chelation therapy with desferrioxamine or oral iron chelation is essential in all patients to minimise iron overload

β-Thalassaemia trait and α-thalassaemia trait
- Can cause diagnostic confusion with mild iron deficiency

α-Thalassaemia major
- Deletion of all 4 α-globin genes, α-thalassaemia major is fatal in utero (Hb Barts) or within hours of birth

Isoimmune
- Haemolytic disease of the newborn

Immune haemolytic anaemia

G6PD deficiency
- Affects over 100 million people worldwide, usually of Mediterranean, Middle East, Far East and Central African ethnicity
- Is X-linked and therefore predominantly affects males, but females may be affected
- May present with neonatal jaundice
- Causes acute intermittent haemolysis precipitated by infection, certain drugs, fava beans (broad beans) and naphthalene in mothballs
- Parents should be given a list of drugs, chemicals and food to avoid

Sickle cell disease
- Family usually originates from tropical Africa or the Caribbean
- Autosomal recessive
- Sickled red cells result in ischaemia in organs or bones
- Main clinical features are: anaemia, infection, painful crises, sequestration crises, splenomegaly in some young children, growth failure, gallstones, behaviour and learning problems
- The most serious clinical complications are bacterial infection, acute chest syndrome, strokes and priapism
- Management: prophylactic penicillin and immunisation; folic acid; maintain good hydration
  Treat crises: analgesia, hydration, antibiotics, exchange or blood transfusion as indicated
  Long-term: hydroxyurea or occasionally bone marrow transplant

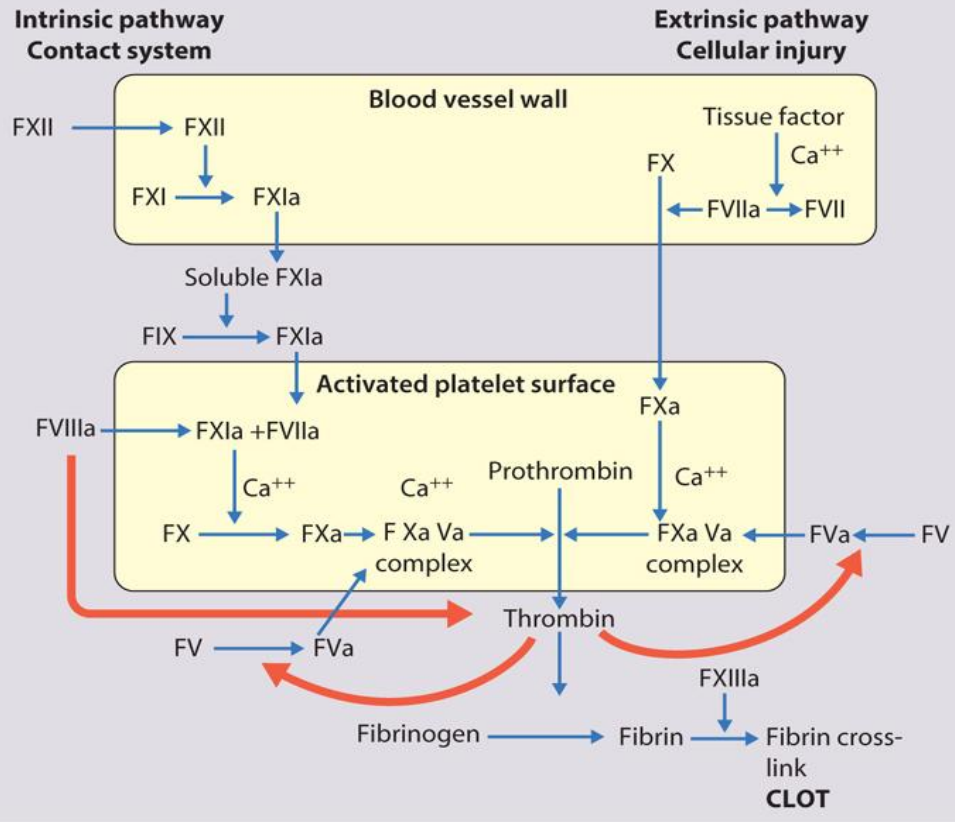


Figure 22.14 Schematic representation of the coagulation pathway.

Box 22.4 Helpful clinical features in evaluating bleeding disorders

Age of onset
- Neonate - in 20% of haemophilias, bleeding occurs in the neonatal period, usually with intracranial haemorrhage or bleeding after circumcision
- Toddler - haemophilias may present when starting to walk
- Adolescent - von Willebrand disease may present with menorrhagia

Family history
- Family tree - detailed family tree required
- Gender of affected relatives (if all boys, suggests haemophilia)

Bleeding history
- Previous surgical procedures and dental extractions - if uncomplicated, suggests bleeding tendency is acquired rather then inherited
- Presence of systemic disorders
- Drug history, e.g. anticoagulants
- Unusual pattern or inconsistent history - consider non-accidental injury

Pattern of bleeding
- Mucous membrane bleeding and skin haemorrhage - characteristic of platelet disorders or von Willebrand disease
- Bleeding into muscles or into joints - characteristic of haemophilia
- Scarring and delayed haemorrhage - suggestive of disorders of connective tissue, e.g. Marfan syndrome, osteogenesis imperfecta or factor XIII deficiency.

Table 22-3. Investigations in haemophilia A and von Willebrand disease

	Haemophilia A	von Willebrand disease
PT	Normal	Normal
APTT	↑↑	↑ or normal
Factor VIII:C	↓↓	↓ or normal
vWF Antigen	Normal	↓
RiCoF (activity)	Normal	↓
Ristocetin-induced platelet aggregation	Normal	Abnormal
vWF multimers	Normal	Variable

PT, prothrombin time; APTT, activated partial thromboplastin time; RiCoF, ristocetin co-factor, measures vWD activity.

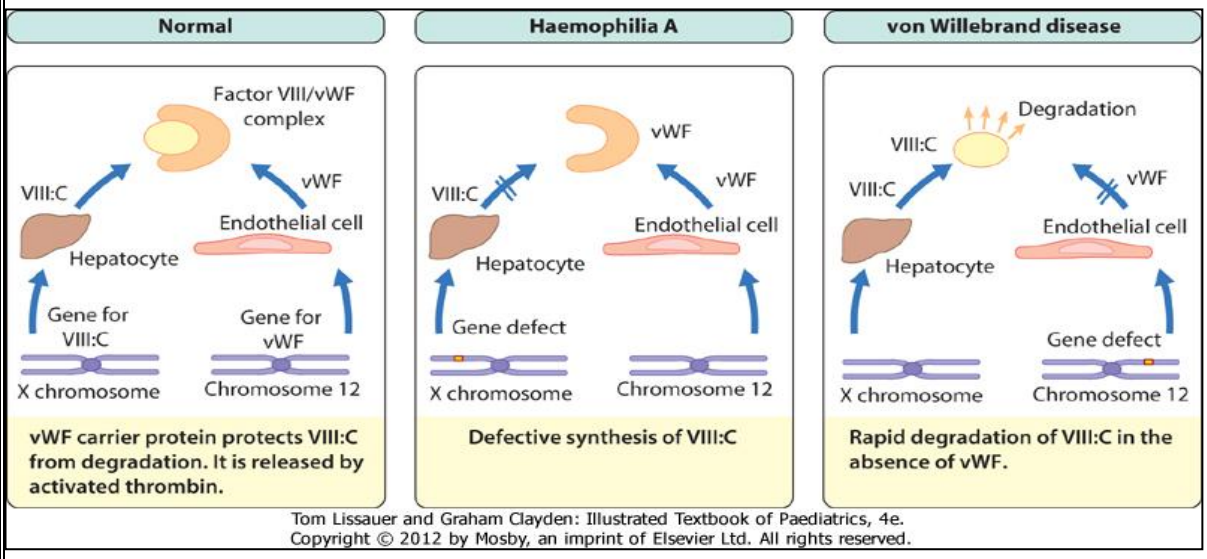


Figure 22.15 Factor VIII synthesis: normal, haemophilia A and von Willebrand disease.

Table 22-4. Severity of haemophilia

Factor VIII:C	Severity	Bleeding tendency
<1%	Severe	Spontaneous joint/muscle bleeds
1-5%	Moderate	Bleed after minor trauma
>5-40%	Mild	Bleed after surgery

Box 22.5 Complications of treatment of haemophilia

Inhibitors, i.e. antibodies to FVIII or FIX
- Develop in 5-20%
- Reduce or completely inhibit the effect of treatment
- Require the use of very high doses of factor VIII or bypassing agents (e.g. FVIIa) for treating bleeding
- May be amenable to immune tolerance induction

Transfusion-transmitted infections
- Hepatitis A, B and C
- HIV
- ?Prions

Vascular access
- Peripheral veins - may be difficult to cannulate
- Central venous access devices may become infected or thrombosed.

The child with abnormal bleeding – into soft tissues, mucocutaneous or following surgery

Acquired disorders

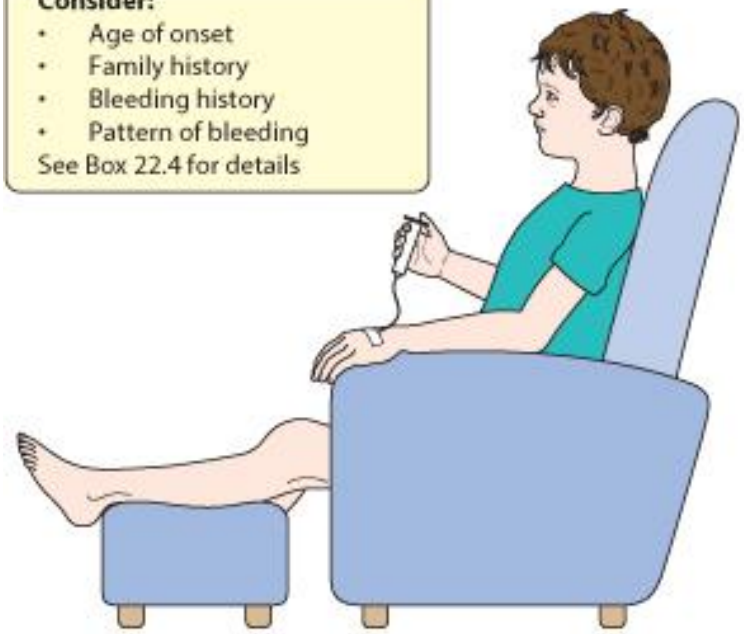
Vitamin K deficiency:
- mainly neonates or early infancy

Liver disease

Thrombocytopenia:
- immune, DIC, etc.

Consider:
- Age of onset
- Family history
- Bleeding history
- Pattern of bleeding

See Box 22.4 for details



Inherited disorders

Haemophilia A (factor VIII deficiency) and haemophilia B (factor IX deficiency):
- Are X-linked recessive disorders affecting males
- Presentation of severe disease – usually with recurrent spontaneous bleeding into joints and muscles at about 1 year of age
- Treatment – recombinant FVIII concentrate for haemophilia A or recombinant FIX concentrate for haemophilia B. Desmopressin (DDAVP) to treat mild haemophilia A
- Treatment complications – inhibitors and intravenous access

von Willebrand disease (vWD):
- Results from either a quantitative or qualitative deficiency of von Willebrand factor (vWF)
- Autosomal dominant
- Presentation – mucosal bleeding, e.g. epistaxis or menorrhagia in adolescence or excessive, prolonged bleeding after surgery
- Treatment – mild disease with DDAVP, severe disease with plasma-derived FVIII concentrate

Table 22-5. Causes of purpura or easy bruising

Platelet count reduced, i.e. thrombocytopenia	
Increased platelet destruction or consumption	
Immune	ITP (immune thrombocytopenia)
	SLE (systemic lupus erythematosus)
	Alloimmune neonatal thrombocytopenia
Non-immune	Haemolytic uraemic syndrome
	Thrombotic thrombocytopenic purpura
	DIC (disseminated intravascular coagulation)
	Congenital heart disease
	Giant haemangiomas (Kasabach-Merritt syndrome)
	Hypersplenism
Impaired platelet production	
Congenital	Fanconi anaemia
	Wiskott-Aldrich syndrome
	Bernard-Soulier syndrome
Acquired	Aplastic anaemia
	Marrow infiltration (e.g. leukaemia)
	Drug-induced
Platelet count normal	
Platelet dysfunction	
Congenital	Rare disorders, e.g. Glanzmann thromboasthenia
Acquired	Uraemia, cardiopulmonary bypass
Vascular disorders	
Congenital	Rare disorders, e.g. Ehlers-Danlos, Marfan syndrome, hereditary haemorrhagic telangiectasia
Acquired	Meningococcal and other severe infections
	Vasculitis, e.g. Henoch-Schönlein purpura, SLE
	Scurvy

Case History 22.3 Immune thrombocytopenic purpura (ITP)

Sian, aged 5 years, developed bruising and a skin rash over 24 h. She had had an upper respiratory tract infection the previous week. On examination she appeared well but had a purpuric skin rash with some bruises on the trunk and legs (Fig. 22.17). There were three blood blisters on her tongue and buccal mucosa, but no fundal haemorrhages, lymphadenopathy or hepatosplenomegaly. Urine was normal on dipsticks testing. A full blood count showed Hb 11.5 g/dl with normal indices, WBC and differential normal, platelet count 17 × 10^9/L. The platelets on the blood film were large; the film was otherwise normal. A diagnosis of ITP was made and she was discharged home. Her parents were counselled and given emergency contact names and telephone numbers. They were also given literature on the condition and advised that she should avoid contact sports but should continue to attend school. Over the next 2 weeks she continued to develop bruising and purpura but was asymptomatic. By the third week, she had no new bruises, and her platelet count was 25 × 10^9/L; the blood count and film showed no new abnormalities. The following week, the platelet count was 74 × 10^9/L and a week later it was 200 × 10^9/L. She was discharged from follow-up.

- **In immune thrombocytopenic purpura, in spite of impressive cutaneous manifestations and extremely low platelet count, the outlook is good and most will remit quickly without any intervention.**

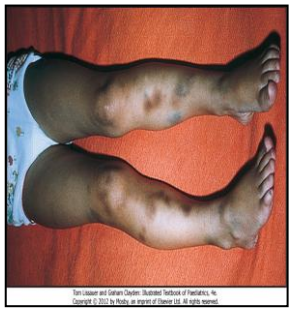


Figure 22.17 Bruising and purpura from immune thrombocytopenic purpura.

The child with petechiae or purpura

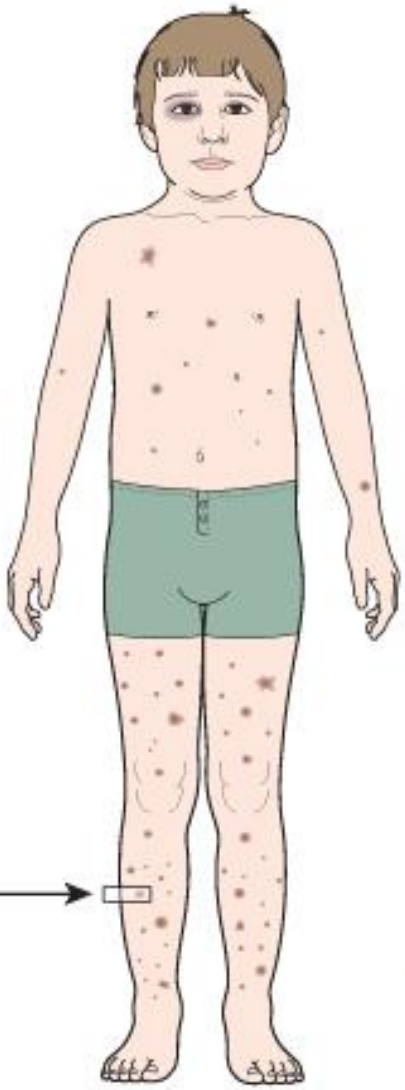
Non-thrombocytopenic

Henoch–Schönlein purpura
- Lesions confined to buttocks, extensor surfaces of legs and arms
- Swollen painful knees and ankles
- Abdominal pain
- Haematuria

Sepsis
- Meningococcal or viral
- Clinical features – fever, septicaemia, meningitis
- If suspected, give parenteral penicillin immediately

Trauma
- Accidental or non-accidental

Other causes (rare)



Positive glass test – rash does not blanch when pressed

Thrombocytopenia

Immune thrombocytopenia (ITP)
- 2–10 years
- Widespread petechiae and purpura and superficial bruising
- Distinguish from acute leukaemia and aplastic anaemia – clinical features, full blood count and blood film
- Bone marrow examination not required if only the platelet count is low, characteristic clinical features and no steroid treatment
- Is acute, benign and self-limiting in about 80% of children
- Treatment – controversial, usually not required unless there is bleeding

Leukaemia
- Clinical features – malaise, infection, pallor, hepatosplenomegaly, lymphadenopathy
- Blood count – also low Hb, blasts on film, confirmed on bone marrow

Disseminated intravascular coagulation (DIC)
- Critically ill – severe sepsis or shock or extensive tissue damage

Other causes (uncommon)

Summary
Thrombosis

All children with thrombosis should be screened for inherited or acquired predisposing disorders.

Chapter 25: Endocrine and metabolic disorders

Box 25.1 Classification of diabetes according to aetiology

- **Type 1. Most childhood diabetes:**
  - - Destruction of pancreatic β-cells by an autoimmune process
- **Type 2. Insulin resistance followed later by β-cell failure:**
  - - Usually older children, obesity-related, positive family history, not as prone to ketosis, commoner in some ethnic groups (e.g. Indian subcontinent)
- **Type 3. Other specific types:**
  - - Genetic defects in β-cell function (maturity-onset diabetes of the young, MODY) due to glucokinase or transcription factor mutations
  - - Genetic defects in insulin action
  - - Infections, e.g. congenital rubella
  - - Drugs, e.g. corticosteroids
  - - Pancreatic exocrine insufficiency, e.g. cystic fibrosis
  - - Endocrine diseases, e.g. Cushing syndrome
  - - Genetic/chromosomal syndromes, e.g. Down and Turner
  - - Neonatal diabetes: transient and permanent
- **Type 4. Gestational diabetes (GDM).**

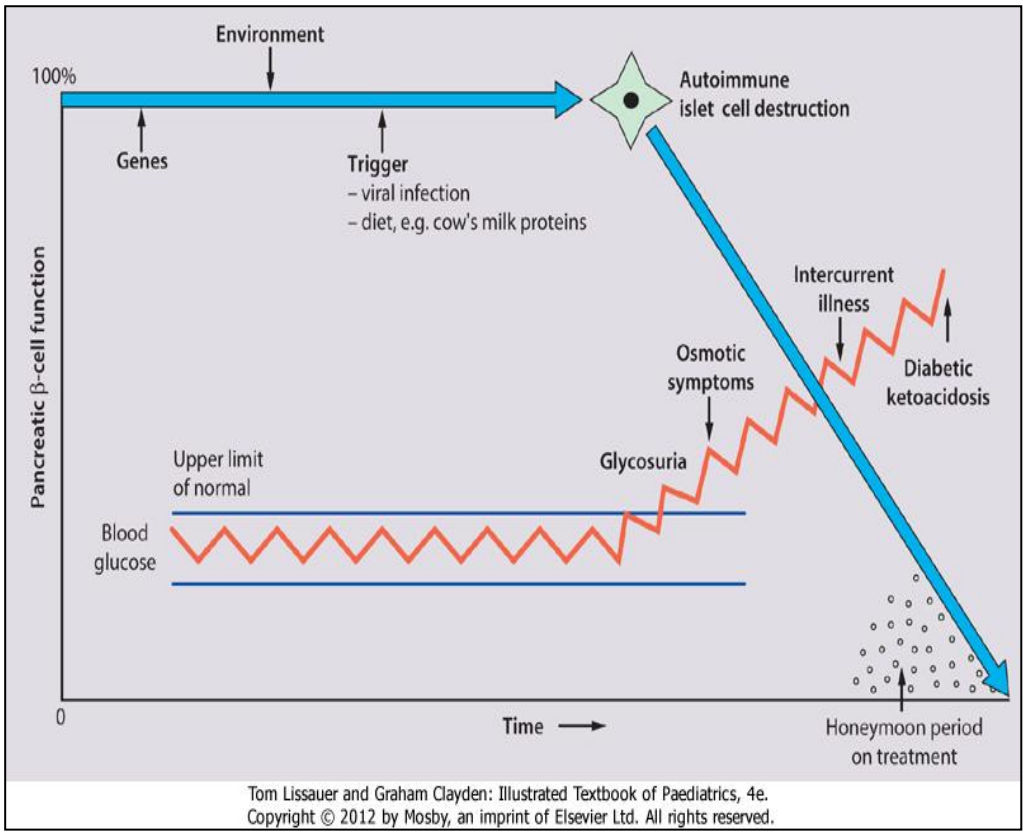


Figure 25.1 Stages in the development of diabetes.

Box 25.2 Symptoms and signs of diabetes

Early

- *Most common - the 'classical triad':*
  - Excessive drinking (polydipsia)
  - Polyuria
  - Weight loss
- *Less common:*
  - Enuresis (secondary)
  - Skin sepsis
  - *Candida* and other infections

Late - diabetic ketoacidosis

- Smell of acetone on breath
- Vomiting
- Dehydration
- Abdominal pain
- Hyperventilation due to acidosis (Kussmaul breathing)
- Hypovolaemic shock
- Drowsiness
- Coma and death.

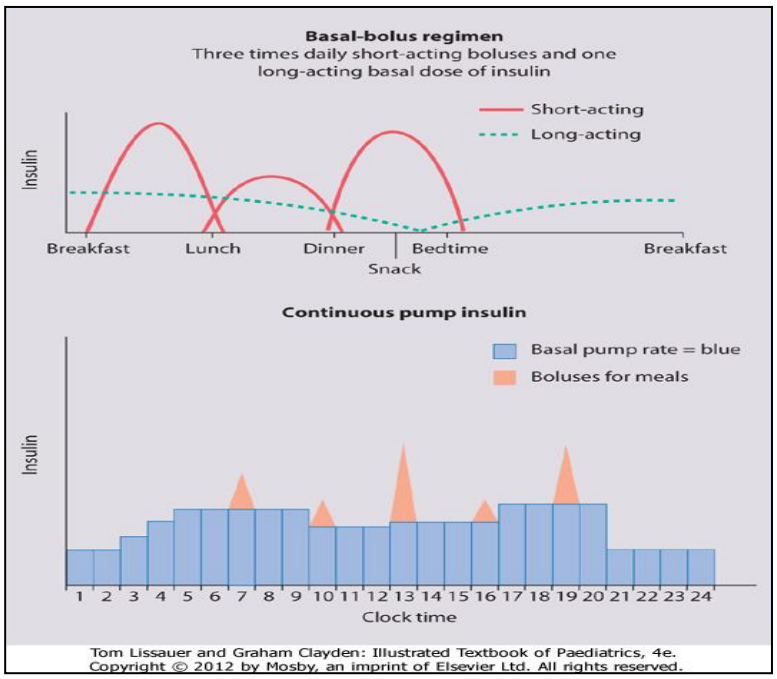


Figure 25.3 Basal-bolus insulin regimen and continuous pump insulin regimen, showing the basal levels of insulin programmed into the pump (blue bars) and the bolus insulin (red pulses) given before each meal/snack according to carbohydrate intake.

Box 25.3 The diabetes team

- Consultant paediatrician(s) with a special interest in diabetes
- Paediatric diabetes specialist nurse(s)
- Paediatric dietician
- Clinical psychologist
- Social worker
- Adult diabetologist for joint adolescent clinics
- Parent/patient support groups.

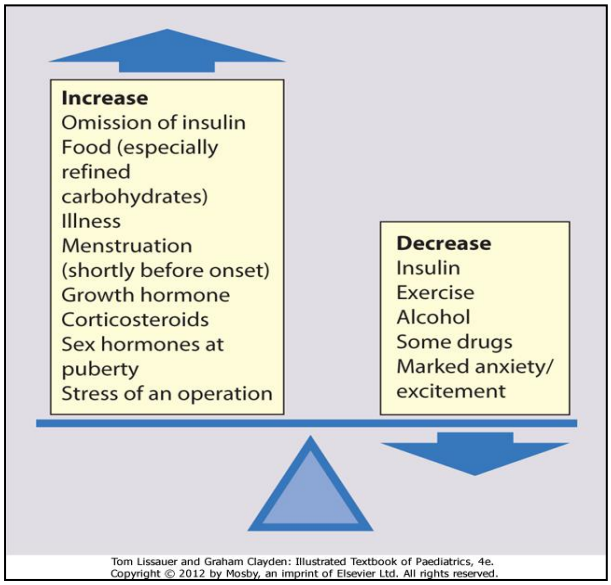


Figure 25.4 Factors affecting blood glucose levels.

Table 25-1. How diabetes interferes with normal adolescence

Normal adolescence	How diabetes interferes
Physical and sexual maturation	Delayed sexual maturation Invasion of privacy with frequent medical examinations
Conformity with peer group	Meals must be eaten on time Frequent injections and blood tests
Self-image	Hypoglycaemic attacks show that they are different
Self-esteem	Impaired body image
Independence from parents	Parental over-protection and reluctance to allow their child to be away from home Battles over diabetes
Economic independence	Loading of insurance premiums Discrimination by employers Statutory rules against becoming a pilot or driving heavy goods or public service vehicles

Diabetic ketoacidosis

Box 25.4 Essential early investigations

- Blood glucose (>11.1 mmol/L)
- Blood ketones (>3.0 mmol/L)
- Urea and electrolytes, creatinine (dehydration)
- Blood gas analysis (severe metabolic acidosis)
- Urinary glucose and ketones (both are present)
- Evidence of a precipitating cause, e.g. infection (blood and urine cultures performed)
- Cardiac monitor for T-wave changes of hypokalaemia
- Weight

Box 25.4 Essential early investigations

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- Blood ketones (>3.0 mmol/L)
- Urea and electrolytes, creatinine (dehydration)
- Blood gas analysis (severe metabolic acidosis)
- Urinary glucose and ketones (both are present)
- Evidence of a precipitating cause, e.g. infection (blood and urine cultures performed)
- Cardiac monitor for T-wave changes of hypokalaemia
- Weight

(b)

(c)

(a) Management priorities

This regimen is initiated if the child is vomiting or has a reduced level of consciousness. Otherwise, even if newly presenting, only subcutaneous insulin is required.

1. Fluids →

If in shock, initial resuscitation is with normal saline. Dehydration should then be corrected gradually over 48–72 h (see Fig. 25.5b and c). Rapid rehydration should be avoided as it may lead to cerebral oedema. Initial rehydration fluids need to be taken into account in calculating fluid requirements. Monitor:

- fluid input and output
- electrolytes, creatinine and acid–base status regularly
- neurological state.

Insert central venous line (CVP) and urinary catheter if shocked.
A nasogastric tube is passed for acute gastric dilatation if there is vomiting or depressed consciousness.

2. Insulin →

Insulin infusion (0.05–0.1 U/kg per h) is started after 1h, titrating the dose according to the blood glucose. Do not give a bolus. Monitor the blood glucose regularly. Aim for gradual reduction of blood glucose of about 2 mmol/h, as rapid reduction is dangerous. Change to 4% dextrose/ 0.18% saline after 24 h when the blood glucose has fallen to 14 mmol/L to avoid hypoglycaemia.

3. Potassium →

Although the initial plasma potassium may be high, it will fall following treatment with insulin and rehydration. Potassium replacement must be instituted as soon as urine is passed. Continuous cardiac monitoring and regular plasma potassium measurements are indicated until the plasma potassium is stable.

4. Acidosis →

Although a metabolic acidosis is present, bicarbonate should be avoided unless the child is shocked or not responding to therapy. The acidosis will self-correct with fluid and insulin therapy. Capillary ketones should be monitored.

5. Re-establish oral fluids, subcutaneous insulin and diet →

Do not stop the intravenous insulin infusion until 1 h after subcutaneous insulin has been given.

6. Identification and treatment of an underlying cause →

Ketoacidosis may be precipitated by an intercurrent infection. Diabetic ketoacidosis causes neutrophilia but not a fever. Antibiotics may be indicated. If the child was known to have diabetes, consider the reason for the ketoacidosis.

Regular assessment of the child with diabetes

Assessment of diabetic control:

- Any episodes of hypoglycaemia, diabetic ketoacidosis, hospital admission?
- Is there still awareness of hypoglycaemia?
- Absence from school? School supportive of diabetes care?
- Interference with normal life?
- HbA_{1c} results – 58 mmol/mol (7.5%) or less?
- Diary of blood glucose results – if monitoring, is he reacting to results?
- Insulin regimen – appropriate? Correction bolus doses given?
- Lipohypertrophy or lipoatrophy (Fig. 25.6a and b) at injection sites?
- Diet – healthy diet, manipulating food intake and insulin to maintain good control?

General overview (periodic):

- Normal growth and pubertal development, avoiding obesity – measure each visit
- Blood pressure check for hypertension yearly (age-specific centiles)
- Renal disease – screening for microalbuminuria yearly from 12 years
- Eyes – photography for retinopathy or cataracts, yearly from 12 years
- Feet – maintaining good care – yearly
- Screening for coeliac and thyroid disease at diagnosis, thyroid screening yearly, coeliac again after 3 years or if weight gain poor.
- Annual reminder to have flu vaccination

Knowledge and psychosocial aspects:

- Good understanding of diabetes, would participation/holidays with other diabetic children be beneficial? Member of Diabetes UK?
- Becoming self-reliant, but appropriate supervision at home, school, diabetic team?
- Taking exercise, sport? Diabetes not interfering with it?
- Leading as normal life as possible?
- Smoking, alcohol?
- Is 'hypo' treatment readily available? Is stepped approach known?
- What are the main issues for the patient? Are there short-term goals to allow engagement with improving control?

(a)

Injection sites – check for lipohypertrophy or lipoatrophy

(b)

Box 25.5 Tests to perform when hypoglycaemia is present

Blood

- Confirm hypoglycaemia with laboratory blood glucose
- Growth hormone, IGF-1, cortisol, insulin, C-peptide, fatty acids, ketones (acetoacetate, 3-hydroxybutyrate), glycerol, branched-chain amino acids, acylcarnitine profile, lactate, pyruvate

First urine after hypoglycaemia

- Organic acids
- Consider saving blood and urine for toxicology, e.g. salicylate, sulphonylurea

Box 25.6 Causes of hypoglycaemia beyond the immediate neonatal period

Fasting

- *Insulin excess*
  - - Excess exogenous insulin, e.g. in diabetes mellitus/insulin given surreptitiously
  - - β-cell tumours/disorders - persistent hypoglycaemic hyperinsulinism of infancy (PHHI, previously called nesidioblastosis), insulinoma
  - - Drug-induced (sulphonylurea)
  - - Autoimmune (insulin receptor antibodies)
  - - Beckwith syndrome
- *Without hyperinsulinaemia*
  - - Liver disease
  - - Ketotic hypoglycaemia of childhood
  - - Inborn errors of metabolism, e.g. glycogen storage disorders
  - - Hormonal deficiency: GH↓, ACTH↓, Addison disease, congenital adrenal hyperplasia

Reactive/non-fasting

- Galactosaemia
- Leucine sensitivity
- Fructose intolerance
- Maternal diabetes
- Hormonal deficiency
- Aspirin/alcohol poisoning.

Summary
Hypoglycaemia

- Should be excluded in any child with septicaemia, who is seriously ill, has a prolonged seizure or altered state of consciousness ('**D**on't **E**ver **F**orget **G**lucose')
- Low blood glucose on bedside testing must be confirmed by laboratory measurement
- If the cause is unknown, diagnostic blood and urine samples should, if possible, be taken at the time.

Box 25.7 Clinical features of hypothyroidism

Congenital	Acquired
Usually asymptomatic and picked up on screening.	Females > males
Otherwise:	Short stature/growth failure
Failure to thrive	Cold intolerance
Feeding problems	Dry skin
Prolonged jaundice	Cold peripheries
Constipation	Bradycardia
Pale, cold, mottled dry skin	Thin, dry hair
Coarse facies	Pale, puffy eyes with loss of eyebrows
Large tongue	Goitre
Hoarse cry	Slow-relaxing reflexes
Goitre (occasionally)	Constipation
Umbilical hernia	Delayed puberty
Delayed development	Obesity
	Slipped upper femoral epiphysis
	Deterioration in school work
	Learning difficulties

Summary
Congenital hypothyroidism

- Is identified on routine neonatal biochemical screening (Guthrie test)
- Although present antenatally, treatment started soon after birth results in satisfactory intellectual development.

Chapter 26: Musculoskeletal disorders

Table 26-3. Causes of polyarthritis

Infection	Bacterial - septicaemia/septic arthritis, TB
	Viral - rubella, mumps, adenovirus, coxsackie B, herpes, hepatitis, parvovirus
	Other - *Mycoplasma*, Lyme disease, rickettsia
	Reactive - gastrointestinal infection, streptococcal infection
	Rheumatic fever
Inflammatory bowel disease	Crohn disease, ulcerative colitis
Vasculitis	Henoch-Schönlein purpura, Kawasaki disease
Haematological disorders	Haemophilia, sickle cell disease
Malignant disorders	Leukaemia, neuroblastoma
Connective tissue disorders	Juvenile idiopathic arthritis (JIA), systemic lupus erythematosus (SLE), dermatomyositis, mixed connective tissue disease (MCTD), polyarteritis nodosa (PAN)
Other	Cystic fibrosis

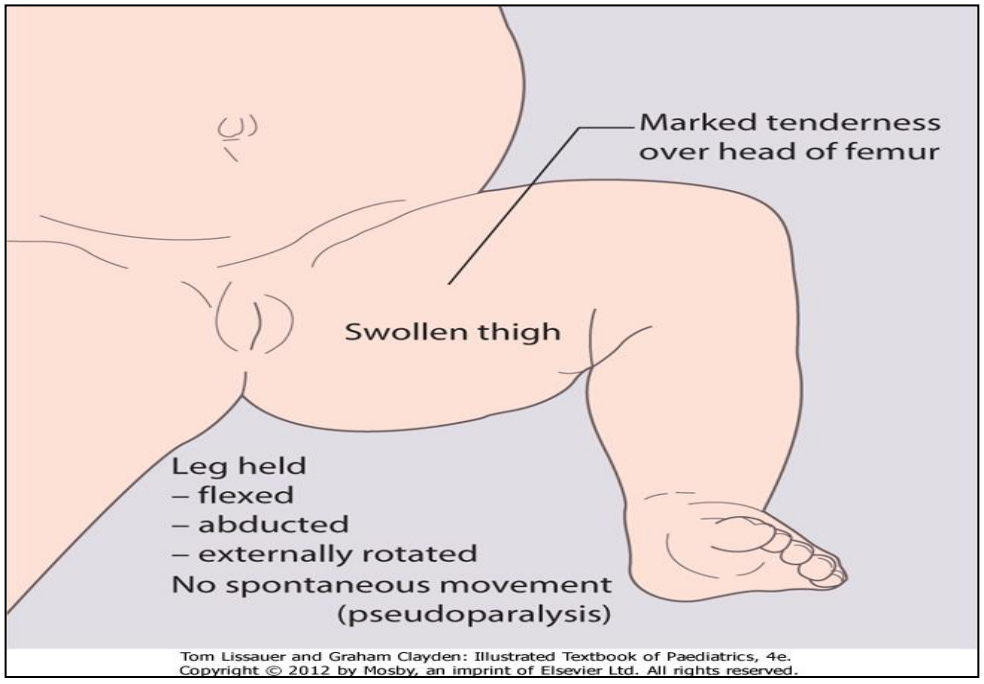


Figure 26.15 Septic arthritis of the hip in infants, showing the characteristic posture to reduce intracapsular pressure. Any leg movement is painful and is resisted.

Table 26-4. Classification and clinical features of JIA (juvenile idiopathic arthritis)

JIA subtype (approximate %)	Onset age	Sex ratio (F : M)	Articular pattern	Extra-articular features	Laboratory abnormalities
Oligoarthritis (persistent) (49%)	1-6 years	5 : 1	1-4 (max) joints involved; knee, ankle or wrist most common	Chronic anterior uveitis in 20%, leg length discrepancy Prognosis excellent	ANA+/-
Oligoarthritis (extended) (8%)	1-6 years	5 : 1	>4 joints involved after first 6 months. Asymmetrical distribution of large and small joints	Chronic anterior uveitis 20%, asymmetrical growth Prognosis moderate	ANA+/-
Polyarthritis (RF negative) (16%)	1-6 years	5 : 1	Symmetrical large and small joint arthritis, often with marked finger involvement Cervical spine and temporomandibular joint may be involved	Low-grade fever, chronic anterior uveitis 5%, late reduction of growth rate Prognosis moderate	
Polyarthritis (RF) positive) (3%)	10-16 years	5 : 1	Symmetrical large and small joint arthritis, often with marked finger involvement	Rheumatoid nodules 10% Similar to adult rheumatoid arthritis Prognosis poor	RF+ (long term)
Systemic arthritis (9%)	1-10 years	1 : 1	Oligoarthritis or polyarthritis. May have aches and pains in joints and muscles (arthralgia/myalgia) but initially no arthritis	Acute illness, malaise, high daily fever initially, with salmon-pink, macular rash, lymphadenopathy, hepatosplenomegaly, serositis Prognosis variable to poor	Anaemia, raised neutrophils and platelets, high acute-phase reactants (see Case History 26.1)
Psoriatic arthritis (7%)	1-16 years	1 : 1	Usually asymmetrical distribution of large and small joints, dactylitis	Psoriasis, nail pitting or dystrophy, chronic anterior uveitis 20% Prognosis moderate	
Enthesitis-related arthritis (7%)	6-16 years	1 : 4	Lower limb, large joint arthritis initially, mild lumbar spine or sacroiliac involvement later on	Enthesitis - localised inflammation at insertion of tendons or ligaments into bone, often in feet, Achilles insertion Occasional acute uveitis Prognosis moderate	HLAB27+
Undifferentiated arthritis (1%)	1-16 years	2 : 1 (variable)	Overlapping articular and extra-articular patterns between ≥2 subtypes or insufficient criteria for sub-classification	Prognosis variable	

Case history 26.1 Systemic –onset juvenile idiopathic arthritis

A 2-year-old boy presented with a high fever (Fig. 26.18a) and malaise. A salmon-coloured rash was present at times of fever (Fig. 26.18b). Investigation showed markedly raised acute-phase reactants. Shortly afterwards, he developed severe polyarthritic joint disease. A diagnosis of systemic-onset juvenile idiopathic arthritis was made on the basis of the clinical presentation and exclusion of other disorders (Table 26.3).

He was treated with high-dose intravenous corticosteroids with rapid improvement, started on oral corticosteroids and weekly methotrexate given by subcutaneous injection. His mother was taught by the nurse specialist how to give the injections to him at home and a daily exercise programme to improve his mobility was provided. A year later he remained on weekly methotrexate. He had persistent problems with his hips, with joint damage on X-ray and may ultimately require hip replacements in his adult years. He is shorter than his peers. He is now at university studying economics and drives his own car.

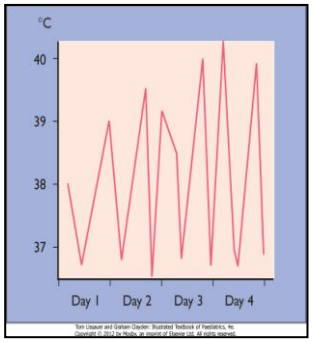


Figure 26.18a Temperature chart.

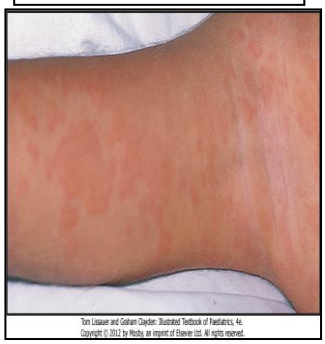


Figure 26.18b Salmon-pink rash.

Summary
Diagnostic clues regarding musculoskeletal disorders

'Typical' symptom combinations	Pivotal clinical features	Possible diagnoses
Nocturnal wakening with leg pain	Normal child	'Growing pains'
		Osteoid osteoma
	Anaemia, bruising, irritability, infections	Leukaemia, lymphoma, neuroblastoma (young child)
'Clunk' on hip movement on screening, limp in an older infant	Asymmetrical upper leg skin folds, limited hip abduction	Developmental dysplasia of the hip (DDH)
Febrile, toxic-looking infant, irritability with nappy changing	Restricted joint range (especially hip)	Septic arthritis Osteomyelitis
Sudden limp in a otherwise well young child	Unilateral restricted hip movement	Transient synovitis of the hip Perthes disease
Fever, erythematous rash, red eyes, irritability in infant or young child	Erythema/oedema of hands and feet, oral mucositis, cervical lymphadenopathy	Kawasaki disease
Irritability, fever, reluctance to move in an infant or young child	Stiff back, 'tripod' sitting	Discitis Vertebral osteomyelitis
Joint pain, stiffness and restriction Loss of joint function	Persistent joint swelling Loss of joint range	Juvenile idiopathic arthritis
Hip pain in an obese adolescent boy	Unilateral hip restriction	Slipped capital femoral epiphysis
Lethargy, unwilling to do physical activities, irritability, rash	Eyelid erythema Proximal muscle weakness	Juvenile dermatomyositis
Constitutional symptoms, lethargy, arthralgia in an adolescent female	Multi-system abnormalities, haematuria, facial erythema	Systemic lupus erythematosus

Chapter 27: Neurological disorders

Box 27.2 Causes of seizures

Epilepsy

- Idiopathic (70-80%) - cause unknown but presumed genetic
- Secondary
  - - Cerebral dysgenesis/malformation
  - - Cerebral vascular occlusion
  - - Cerebral damage, e.g. congenital infection, hypoxic-ischaemic encephalopathy, intraventricular haemorrhage/ischaemia
- Cerebral tumour
- Neurodegenerative disorders
- Neurocutaneous syndromes

Non-epileptic

- Febrile seizures
- Metabolic
  - - Hypoglycaemia
  - - Hypocalcaemia/hypomagnesaemia
  - - Hypo/hypernatraemia
- Head trauma
- Meningitis/encephalitis
- Poisons/toxins.

Summary
Breath-holding and reflex anoxic seizures

In toddlers:

- Breath-holding episodes - toddler, precipitated by anger, holds breath, goes blue, then limp, rapid recovery
- Reflex anoxic seizures - toddler, precipitated by pain, stops breathing, goes pale, brief seizure sometimes, rapid recovery
- Other non-epileptic paroxysmal disorders: see Fig. 27.1.

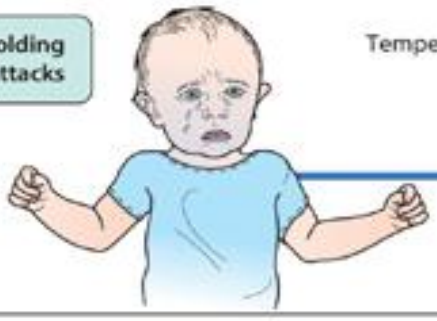
Summary
Febrile seizures

- Affect 3% of children; have a genetic predisposition
- Occur between 6 months and 6 years of age
- Are usually brief, generalised tonic-clonic seizures occurring with a rapid rise in fever
- If a bacterial infection, especially meningitis, is present, it needs to be identified and treated
- Advise family about management of seizures, consider rescue therapy
- If simple - does not affect intellectual performance or risk of developing epilepsy
- If complex, 4-12% risk of subsequent epilepsy.

Causes of funny turns

Breath-holding attacks

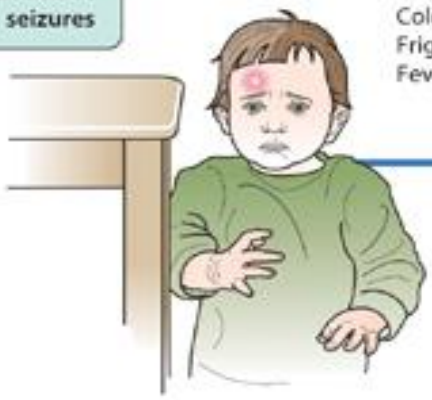
Temper



Occur in some toddlers when they are upset. The child cries, holds his breath and goes blue. Sometimes children will briefly lose consciousness but rapidly recover fully. Drug therapy is unhelpful. Attacks resolve spontaneously, but behaviour modification therapy, with distraction, may help.

Reflex anoxic seizures

Head trauma
Cold food
Fright
Fever



Occur in infants or toddlers. Many have a first-degree relative with a history of faints. Commonest triggers are pain or discomfort, particularly from minor head trauma, cold food (such as ice-cream or cold drinks), fright or fever. Some children with febrile seizures may have experienced this phenomenon. After the triggering event, the child becomes very pale and falls to the floor. The hypoxia may induce a generalised tonic–clonic seizure. The episodes are due to cardiac asystole from vagal inhibition. The seizure is brief and the child rapidly recovers. Ocular compression under controlled conditions often leads to asystole and paroxysmal slow-wave discharge on the EEG.

Syncope

Children may faint if in a hot and stuffy environment, on standing for long periods, or from fear. Clonic movements may occur.

Migraine

May sometimes lead to paroxysmal headache involving unsteadiness or light-headedness as well as the more common visual or gastrointestinal disturbance. In some young people these episodes occur without headache.

Benign paroxysmal vertigo

This is characterised by recurrent episodes of vertigo, lasting from one to several minutes, associated with nystagmus, unsteadiness or even falling. It is a primary headache disorder of childhood occasionally due to a viral labyrinthitis.

Other causes

Cardiac arrhythmia – prolonged QT interval may rarely cause collapse or cardiac syncope which may be related to exercise
Tics, daydreaming, night terrors
Self-gratification – young children may stimulate their genitalia in order to achieve a feeling of comfort rather than sexual gratification
Non-epileptic attack disorder (NEAD)
Pseudoseizures – when children feign seizures
Fabricated – seizures are fabricated by parent
Induced illness (non-accidental injury) – e.g. seizures, from hypoglycaemia from an adult deliberately injecting insulin
Paroxysmal movement disorders – well-circumscribed episodes, genetically determined, no loss of consciousness.

Epilepsy seizure types

Generalised seizures

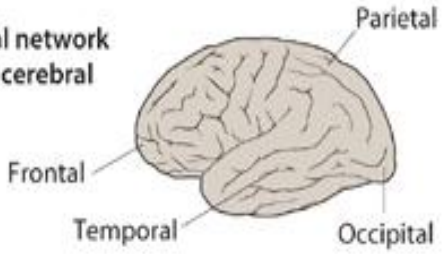
Onset in both hemisphere

In generalised seizure disorders, there is:
- always a loss of consciousness
- no warning
- symmetrical seizure
- bilaterally synchronous seizure discharge on EEG or varying asymmetry

Absence seizures	Transient loss of consciousness, with an abrupt onset and termination, unaccompanied by motor phenomena except for some flickering of the eyelids and minor alteration in muscle tone. Absences may be typical (petit mal) or atypical and can often be precipitated by hyperventilation
Myoclonic seizures	Brief, often repetitive, jerking movements of the limbs, neck or trunk Non-epileptic myoclonic movements are also seen physiologically in hiccoughs (myoclonus of the diaphragm) or on passing through stage II sleep (sleep myoclonus)
Tonic seizures	Generalised increase in tone
Tonic–clonic seizures	Rhythmical contraction of muscle groups following the tonic phase. In the rigid tonic phase, children may fall to the ground, sometimes injuring themselves. They do not breathe and become cyanosed. This is followed by the clonic phase, with jerking of the limbs. Breathing is irregular, cyanosis persists and saliva may accumulate in the mouth. There may be biting of the tongue and incontinence of urine. The seizure usually lasts from a few seconds to minutes, followed by unconsciousness or deep sleep for up to several hours
Atonic seizures	Often combined with a myoclonic jerk, followed by a transient loss of muscle tone causing a sudden fall to the floor or drop of the head

Focal seizures

Onset in neural network limited to one cerebral hemisphere



Focal seizures:
- begin in a relatively small group of dysfunctional neurones in one of the cerebral hemispheres
- may be heralded by an aura which reflects the site of origin
- may or may not be associated with change in consciousness or more generalised tonic-clonic seizure

Focal seizures	Frontal seizures – motor phenomena Temporal lobe seizures – auditory or sensory (smell or taste) phenomena Occipital – positive or negative visual phenomena Parietal lobe seizures – contralateral altered sensation (dysaesthesia)

Table 27-1. Some epilepsy syndromes - arranged by age of onset

Name	Age	Seizure pattern	Comments
West syndrome	4-6 months	Violent flexor spasms of the head, trunk and limbs followed by extension of the arms (so-called 'salaam spasms'). Flexor spasms last 1-2 s, often multiple bursts of 20-30 spasms, often on waking, but may occur many times a day. May be misinterpreted as colic. Social interaction often deteriorates - a useful marker in the history	Many causes; two-thirds have underlying neurological cause. The EEG shows hypsarrhythmia, a chaotic pattern of high-voltage slow waves, and multi-focal sharp wave discharges (Fig. 27.3). Treatment is with vigabatrin or corticosteroids; good response in 30-40%, but unwanted effects are common. Most will subsequently lose skills and develop learning disability or epilepsy
Lennox-Gastaut syndrome	1-3 years	Multiple seizure types, but mostly drop attacks (astatic seizures), tonic seizures and atypical absences. Also neurodevelopmental arrest or regression and behaviour disorder	Often other complex neurological problems or history of infantile spasms. Prognosis is poor
Childhood absence epilepsy	4-12 years	Stare momentarily and stop moving, may twitch their eyelids or a hand minimally. Lasts only a few seconds and certainly not longer than 30 s. Child has no recall except realises they have missed something and may look puzzled or say 'pardon' on regaining consciousness. Developmentally normal but can interfere with schooling. Accounts for only 2% of childhood epilepsy	Two-thirds are female. The episodes can be induced by hyperventilation, the child being asked to blow on a piece of paper or windmill for 2-3 min, a useful test in the outpatient clinic. The EEG shows generalised 3/second spike and wave discharge, which is bilaterally synchronous during and sometimes between episodes (Fig. 27.4). Prognosis is good, with 95% remission in adolescence; 5-10% may develop tonic-clonic seizures in adult life
Benign* epilepsy, with centrotemporal spikes (BECTS)	4-10 years	Tonic-clonic seizures in sleep, or simple focal seizures with awareness of abnormal feelings in the tongue and distortion of the face (supplied by the Rolandic area of the brain)	Comprises 15% of all childhood epilepsies. EEG shows focal sharp waves from the Rolandic or centrotemporal area. Important to recognise as it is benign and does not always require treatment. Almost all remit in adolescence
Early-onset benign* childhood occipital epilepsy (Panayiotopoulos type)	1-14 years	Younger children - periods of unresponsiveness, eye deviation, vomiting and autonomic features. Older children - headache and visual disturbance including distortion of images and hallucinations	Uncommon. EEG shows occipital discharges. Remit in childhood
Juvenile myoclonic epilepsy	Adolescence-adulthood	Myoclonic seizures, but generalised tonic-clonic seizures and absences may occur, mostly shortly after waking. A typical history is throwing drinks or cornflakes about in the morning as myoclonus occurs at this time. Learning is unimpaired	Characteristic EEG. Response to treatment is usually good but lifelong. A genetic linkage has been identified. Remission unlikely

*Although called benign, may be specific learning difficulties in some children.

Table 27-2. Choice of anti-epileptic drugs (NICE 2004)

Seizure type	First-line	Second-line
Generalised seizures		
Tonic-clonic	Valproate, carbamazepine	Lamotrigine, topiramate
Absence	Valproate, ethosuximide	Lamotrigine
Myoclonic	Valproate	Lamotrigine
Focal seizures	Carbamazepine, valproate Lamotrigine shown since to be most effective - but slow titration	Topiramate, levetiracetam, oxcarbazepine, gabapentin, tiagabine, vigabatrin

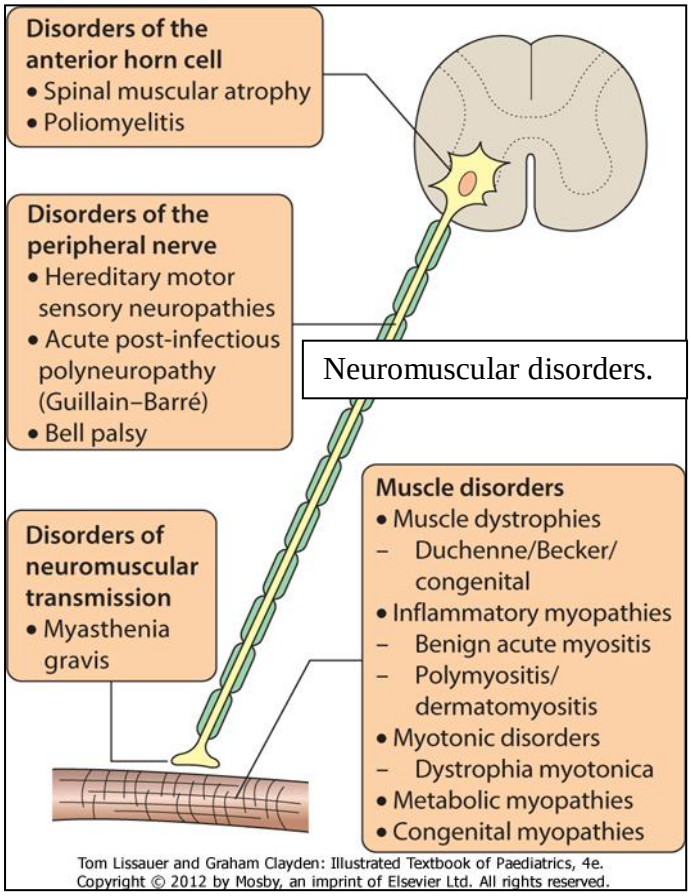
Table 27-3. Common or important unwanted effects of anti-epileptic drugs

Drug	Side-effects
Valproate	Weight gain, hair loss
	Rare idiosyncratic liver failure
Carbamazepine/oxcarbazepine	Rash, neutropenia, hyponatraemia, ataxia
	Liver enzyme induction, can interfere with other medication
Vigabatrin	Restriction of visual fields, which has limited its use
	Sedation
Lamotrigine	Rash
Ethosuximide	Nausea and vomiting
Topiramate	Drowsiness, withdrawal and weight loss
Gabapentin	Insomnia
Levetiracetam	Sedation - rare
Benzodiazepines - clobazam, clonazepam, diazepam, nitrazepam	Sedation, tolerance to effect, increased secretions

All the above may cause drowsiness and occasional skin rashes.

Summary
Epilepsy

- Affects 1 in 200 children
- Classified according to seizure type; the identification of a syndrome, where possible; and underlying aetiology
- If suspected, an EEG is indicated
- Anti-epileptic drug therapy should be considered where the seizures are intrusive, selected according to seizure type, monotherapy if possible and with the least potential for unwanted effects
- Requires liaison with the school about the management of seizures and avoiding situations which could lead to injury.



Box 27.3 Causes of the floppy (hypotonic) infant

Central

Cortical

- Hypoxic-ischaemic encephalopathy
- Cortical malformations

Genetic

- Down syndrome
- Prader-Willi syndrome

Metabolic

- Hypothyroidism
- Hypocalcaemia

Peripheral

Neuromuscular

- Spinal muscular atrophy
- Myopathy
- Myotonia
- Congenital myasthenia.

Summary
Neuromuscular disorders

- Present with muscle weakness, which may manifest with floppiness, delayed motor milestones, unsteady gait or muscle fatiguability
- Anterior horn cell - *spinal muscular atrophy*: progressive weakness and wasting of skeletal muscles; tongue fasciculation may aid diagnosis
- Peripheral nerve
  - - *Hereditary motor sensory neuropathies* (HMSN): symmetrical wasting of the distal muscles
  - - *Acute post-infectious polyneuropathy* (Guillain-Barré syndrome): ascending symmetrical weakness; may be bulbar palsy and respiratory depression
- Neuromuscular transmission - *juvenile myasthenia*: >10 years old, ophthalmoplegia and ptosis, loss of facial expression and difficulty chewing
- Muscle - *Duchenne muscular dystrophy*: X-linked recessive, presents with waddling gait and difficulty climbing stairs

Summary
Hydrocephalus

- In infants, presents with excessive increase in head circumference, separation of skull sutures, bulging of the anterior fontanelle, distension of scalp veins and sun setting of the eyes
- Older children present with raised intracranial pressure
- Treatment is usually with a ventriculo-peritoneal shunt.

Box 27.4 Causes of hydrocephalus
Non-communicating (obstruction in the ventricular system)

Congenital malformation

- Aqueduct stenosis
- Atresia of the outflow foramina of the fourth ventricle (Dandy-Walker malformation)
- Chiari malformation

Posterior fossa neoplasm or vascular malformation

Intraventricular haemorrhage in preterm infant

Communicating (failure to reabsorb CSF)

Subarachnoid haemorrhage

Meningitis, e.g. pneumococcal, tuberculous

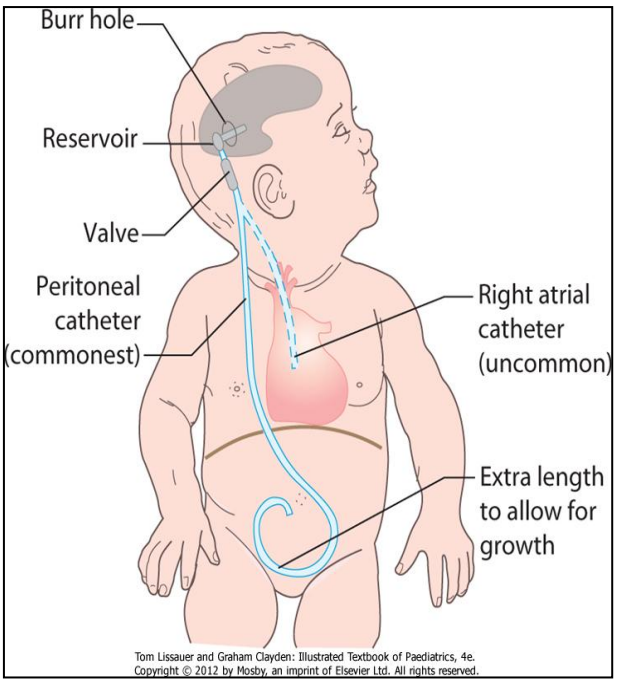


Figure 27.17 Ventriculoperitoneal shunt for drainage of symptomatic hydrocephalus. A sufficient length of shunt tubing is left in the peritoneal cavity to allow for the child's growth. Right atrial catheters require revision with growth.